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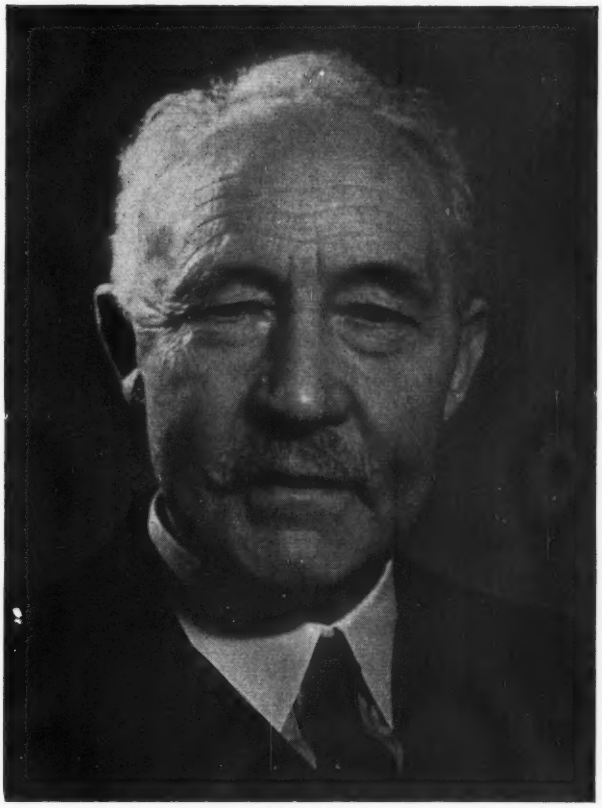
GEORGE ERNEST GASK

C.M.G., D.S.O., M.A., F.R.C.S.

PROFESSOR GEORGE ERNEST GASK is an idealist, and as idealism is an inborn, not an acquired, character, it may be assumed that for seventy-five years he has been steadily radiating the quiet kindliness which is remembered by so many of his pupils and colleagues. Gask was born on Aug. 1, 1875, and received his early education at Dulwich College. He then spent some months at Lausanne and Freiburg-i-Baden, before entering the medical school of St. Bartholomew's Hospital in 1893. He qualified five years later, obtaining the Fellowship of the Royal College of Surgeons of England in 1901. At his hospital he steadily ascended the rungs of the usual ladder, starting as house surgeon to John Langton, and was elected to the surgical staff of the hospital in 1907. He had also been appointed Warden of the Medical College in 1906, and lived for several years in the Warden's House in the hospital. The outbreak of the first world war in 1914 found him well established as a London consultant, with a practice in general surgery, and a special interest in the surgery of the chest. During the war he served in the R.A.M.C. successively as a Captain attached to No. 1 General Hospital, as a Surgical Specialist with the rank of Major at a Casualty Clearing Station in France, and finally as Consulting Surgeon to the Fourth Army with the rank of Temporary Colonel, A.M.S. For his distinguished services he was four times mentioned in despatches, was given the D.S.O. in 1917, and was made C.M.G. in 1919. His special interest in the surgery of the chest he carried on through the war years and did much to improve and develop the treatment of thoracic injuries.

Gask had always been much more than a surgical technician, and medical education was one of his major interests. So, for some years before the first world war, he had been pondering the idea of the Professorial Unit as part of a teaching hospital, and, therefore, seized eagerly the opportunity offered to him as soon as the war was over of becoming Director of the first Professorial Unit at his own hospital. Here was an opportunity for his idealism to have an outlet, and he cheerfully abandoned all private practice, devoting himself wholeheartedly to making the professorial system work. By steadily pursuing his ideal without rashly or unnecessarily challenging the established order, Gask had, in a few years, demonstrated that even in a reputedly conservative institution the new system could be a triumphant success. Similar units elsewhere had difficult times and some were abandoned as failures, but Gask's unit under his imperturbable leadership justified his own faith and served as a pattern to others.



GEORGE ERNEST GASK

Gask's success could never be ascribed to his being either "clever" or "brilliant". These sometimes shallow attributes would not have guided him so well through the shoals of the experimental period as did his utter honesty of purpose, his habit of never acting except after careful thought, and his capacity for leading his team with wisdom and understanding. He believed firmly in the value of seeing other men at work in other places, and he led his associates to all the important surgical centres in England and Scotland, and his senior colleagues, as a body of Pilgrim Surgeons, to the clinics all over Europe—himself acting as organizer and courier—

again the Practical Idealist. As an operator Gask used a technique which, though anything but showy, was always sensible and gentle, and imperturbability was never better exemplified than by the spectacle of Gask in difficulties. His movements would then become more and more deliberate, and a really desperate situation would be the signal for packing off the wound and smoking a mental cigarette. His younger assistants he would instruct never to run or even hurry across the Hospital Square. No emergency, he would imply, could justify so hasty an approach. If the surgeon was not calm, the patient would suffer, and Gask's consideration for his patients, though never mentioned in a sententious or complacent way, was always near the surface of his mind.

Gask's association with the BRITISH JOURNAL OF SURGERY began with his election to the Editorial Committee in July, 1919, and to the sub-committee now known as the Executive Committee. Moynihan was the Chairman, supported by Rickman Godlee, Makins, D'Arcy Power, Sherren, Burghard, Corner, Raymond Johnson, Thorburn, Waugh, and Hey Groves. For many years the course of the JOURNAL ran smoothly, with Moynihan at the helm and Hey Groves as Secretary. Gask's influence, however, was making itself felt, and when in October, 1934, Moynihan suggested resigning the Chairmanship because of his enforced absences from London, the Editorial Committee turned naturally to Gask, asking him to become Vice-Chairman and to take charge of all sub-committees. So it was that in May, 1935, Gask presided over a sub-committee with D'Arcy Power, Fagge, Miles, Burgess, Martin, and Hey Groves, to consider the matter of a Moynihan testimonial. It was then decided that money should be collected, perhaps for the equipment of an animal operating theatre at the Royal College, and that a special Moynihan issue of the Journal should be put in hand under the care of Gask, Fagge, and Hey Groves.

It was about the same time that Gask asked a number of his friends if they would approve the idea of fashioning in silver a statuette of a young man holding above his head a book representing the JOURNAL OF SURGERY. Gask had long been deeply interested in the craft of the silversmith, and ultimately the statuette was made by his favourite craftsman, Omar Ramsden, at the cost of £100. This fine piece of work was presented to Moynihan on July 6, 1936, at the Royal College of Surgeons. Moynihan was much gratified, and announced his intention of having a replica made to be placed on the table at meetings of the Editorial Committee. His death took place, however, before this was finished and his son, the present Lord Moynihan, presented the reproduction of the statuette to the JOURNAL; it now stands on the table at all meetings, a reminder both of the Founder and of the Vice-Chairman (appointed Chairman in October, 1936) who wished to honour him. Gask held the office of Chairman for ten years, and in April, 1947, his services were commemorated by the presentation of a silver skewer, and in receiving this Gask was no doubt speaking no more than the truth when he said that he had never enjoyed any meetings more than those of the Editorial Committee of the JOURNAL.

In directing the affairs of the JOURNAL Gask showed again his capacity for the quiet and effective management of his fellow men, and for the broad-minded enrolment of all who could help in forwarding the interests of British Surgery. He was always internationally-minded, and valued especially every contact that could be made with the surgeons of the New World. He, therefore, arranged for the appointment of Elliot Cutler, Consulting Surgeon to the American Forces in Europe, to the Editorial Committee, and later enlarged its scope by adding representatives of Anæsthetics, Pathology, Ophthalmology, and even Industrial Medicine. He believed also that, in addition to the Teaching Hospitals, the Provincial and Municipal non-Teaching Hospitals should be represented. When Hey Groves resigned the office of Secretary in 1941, a still greater responsibility rested upon Gask with Martin and Wakeley as his adjutants, and it was this team that was chiefly responsible for carrying the JOURNAL safely through the difficult war years and into the only slightly less difficult days following the war. They arranged also for the first special war numbers on Penicillin and Neuro-surgery.

When Gask retired from his many public duties in 1935 he no doubt supposed that he would spend much of his time at his favourite pursuit of gardening at his home in the Chilterns, but his respite was brief. He was soon appointed Justice of the Peace for Buckinghamshire and a Rural District Councillor. Soon after the outbreak of war in 1939 he returned to temporary duty as surgeon to the Radcliffe Infirmary, Oxford, and Lecturer in the University. Later he became Adviser in Surgery for Region VI of the Emergency Medical Service, and worked also for the Nuffield Provincial Hospitals Trust and the Buckinghamshire and Oxfordshire Regional Hospitals Council. The introduction of the National Health Service naturally led to his taking a large part in the work of the Regional Board, and so the tale of his distinguished public services continued until the warning came for the necessary curtailment of his ceaseless activity. Gask's physique is of the sturdiest type, and his love of mountaineering with his careful and sure-footed technique has been typical of his way through life—whether in teaching the young idea at Bart's, in the operating theatre, or in the countless committee meetings, at which he would so unobtrusively steer others round to his own way of thinking. No one could have accomplished so much in influencing the trend of affairs without a certain modicum of inflexibility. An Idealist, to be successful, has to be both practical and obstinate. Gask can be all three at once, and the success of this JOURNAL owes, next to Moynihan and Hey Groves, as much to him as to any. This issue of the JOURNAL is, therefore, dedicated to him with the gratitude and affection of all his colleagues to mark the passage of years and the attainment of his seventy-fifth birthday.

SMOOTH-MUSCLE TUMOURS OF THE GASTRO-INTESTINAL TRACT

By R. H. COWDELL

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MANY reports have appeared in the literature of small numbers of cases of tumours of the gastro-intestinal tract derived from smooth muscle tissue, and there have been excellent reviews. Neuber (1920) cites Morgagni (1761) as having reported a probable instance, but a perusal of his writings (Morgagni, 1769), while revealing several tumours of the stomach, one of them apparently pedunculated, intragastric, and centrally necrotic, gives no very convincing evidence that all are not carcinomata. Golden and Stout (1941) examined 400 publications involving 1018 cases, and reported 60 examples of their own. Pack and McNeer (1935) had previously reviewed cases of gastric sarcomata to that date and reported a further 9 cases. It is still apparent, however, that the possibility of such tumours often fails to come to mind during diagnosis, and it is felt that if it were more widely recognized, and confusion with carcinomata were reduced, operative cure might be possible in some cases now regarded as hopeless, and less radical measures might suffice in some of the more localized tumours.

This paper reports 10 cases, of which 9 are tumours of the stomach and 1 of the jejunum, with the addition of a hamartoma of the duodenum which was clinically of considerable interest and which contained a large proportion of smooth muscle tissue. The material represents those leiomyomatous tumours which have been examined in the Department of Pathology of the Radcliffe Infirmary during the period April, 1938–April, 1949. Of the total, 6 were treated by operative removal, and although in several instances the post-operative period is still short, the outcome in each has so far been very satisfactory. One (*Case* 7) was examined by laparotomy during life, and, although the condition was thought to be a sarcoma, it appeared inoperable and death followed within five months. Two (*Cases* 6 and 8) were first revealed in their true light post mortem. The remaining two were small tumours which were incidental findings at autopsy and were not likely to have been responsible for symptoms during life. Such small leiomyomata are not uncommon, and as many of them are only a few millimetres in diameter, they are probably not infrequently missed during routine post-mortem examination. As an illustration of their relative frequency, Rieniets (1930) reported an incidence of 16 per cent in 200 consecutive autopsies at the Mayo Clinic. While histologically benign, they are of interest in that they might eventually have caused symptoms, but it is not proposed to enlarge greatly on them here, but rather to concentrate on those directly responsible for admission to hospital.

INCIDENCE

The population of the area served by this hospital during the period under consideration has been about one million, and the total admissions during the eleven years, 1938–49 inclusive, number 108,937. Of these, 370 were found to have tumours of the stomach, 84 dying while in hospital. The 9 leiomyomata and leiomyosarcomata of the stomach here reported represent 2·4 per cent of the gastric neoplasms, a proportion which, while fairly small, cannot be considered negligible. Strictly comparable incidence rates are difficult to find, but Pack and McNeer (1935) give the proportion of sarcomata as 1 per cent of malignant gastric neoplasms, and state that this is a commonly quoted frequency, while Fenwick (1901) reported an incidence of 5 to 8 per cent, which the above authors regard as questionable. These figures include all sarcomata, and, in their own series, D'Aunoy and Zoeller (1930) found 6 per cent of muscle tumours, while Lubarsch and Henhe (1926) found 16 per cent. All the series are relatively small, but our figures, while including a proportion of benign tumours, appear appreciable higher than the average.

PATHOLOGY

The tumours arise from muscular tissue in the gastro-intestinal tract, and very occasionally derivation may be seen to be from the muscularis mucosæ, as in one of the cases of Golden and Stout (1941, *Case* 36). Two main forms occur, both being usually firm, rounded, or lobulated greyish masses. These were first separated by Virchow (1863), who described them as *inneren* (intragastric) and *ausseren* (extragastric). The small flat tumours revealed incidentally at post mortem often fall into a third, intramural, group. The intragastric type is usually sessile, so that the gross and radiological appearances are almost indistinguishable during life from carcinomata. Such tumours may sometimes have clearly-defined margins, but not infrequently infiltrate with a much more ragged edge which may be difficult to define and cause wide excision to be necessary. Occasionally an intragastric tumour is pedunculated, *Case* 1 being an example with a wide pedicle. Pedunculation within the lumen of the gut is more common in the small intestine. The extragastric type may be sessile but is more frequently pedunculated. Central degeneration is common, with hyaline change, cyst formation, hæmorrhage, necrosis, and calcification. They may reach a great size, having been reported as weighing up to 6500 g., and many large vessels frequently course over the peritoneal surface. There may be mucosal ulceration with all types, though in many of the extragastric tumours the mucosa is intact.

Golden and Stout (1941) advocate biopsy as a method by which a fair estimate of malignancy can be reached, but although the method has not been used here, it appears that it would give rise to very considerable difficulty, in that many of the usual histological criteria are not satisfactory guides to clinical behaviour, and variation of pattern between different parts of the same tumour may be great (*Case* 4), so that sections from different areas would

result in extremely dissimilar reports. In only one of our cases (*Case* 7) have metastases been found, and these have usually been reported as late occurrences, so that complete excision of the primary tumour offers a good prognosis. Further, in this case it is almost certain that a biopsy specimen would have been reported as histologically benign. Giant cells with one or more nuclei have been found in nearly all the tumours except the small incidental ones, and in several mitoses are common, without any apparently very close correlation with rate or degree of extension. Frequency of mitoses remains, however, the most valuable single criterion of malignancy. In the better-differentiated tumours there is often a striking tendency towards palisade formation of the nuclei, and confusion with neurilemmomata may easily occur (Gosset, Bertrand, and Loewy, 1924; Tierney, 1934; Ransom and Kay, 1940). Golden and Stout (1941) reclassified as leiomyomata three tumours previously reported by Stout (1935) as of nerve-sheath origin.

It would appear that biopsy in many instances would only be of value in confirming that the tumour was of muscular and not of epithelial origin, in cases where its form leaves this in doubt. In most instances, however, the origin of the tumour is rendered almost certain by its typical macroscopic appearance.

Five of our cases have been classified as histologically malignant and 5 as benign. There is a tendency to marginal infiltration for a variable distance in many instances, which may result in inoperability, but the distinction between malignant leiomyomata, which showed local invasion, and leiomyosarcomata, with distant spread, suggested by Ghon and Hintz (1909) appears artificial. It would seem that any leiomyoma may eventually show malignant characteristics, but that on the whole tumour development and extension is slower and less wide than in carcinomata. The series reported here is not sufficiently extensive to justify statistical treatment of such considerations as the incidence of metastases. However, Golden and Stout (1941) report an incidence of some 30 per cent in histologically malignant tumours. Metastases occur most commonly in the liver, while they have also been reported in the lung and peritoneum, and in the regional lymph-nodes (Cellina, 1931; Brink and Laing, 1933; Pack and McNeer, 1935; Gottlieb and Reitman, 1939). Cases of histologically benign leiomyomata associated with metastases (Hunt, 1923; Demel, 1926; Melnick, 1932) further emphasize the difficulty of histological assessment by biopsy. Generalized metastases to distant organs are rare, but have been found in one case each by Pack and McNeer (1935) and by Ghon and Hintz (1909).

SYMPTOMATOLOGY

This is extremely variable and may imitate a wide variety of conditions, while some cases are clinically indistinguishable from carcinomata. Hæmorrhage may occur into the lumen of the stomach or into the peritoneal cavity. The former is more common with intragastric tumours, and may be sudden and massive or more gradual, giving rise to hæmatemesis, melæna, or slowly progressive anæmia. Some degree of ulceration and bleeding is usual with the intragastric type, while with the extragastric tumours the mucosa is frequently intact although ulceration may occur. An example is given in one of our cases (*Case* 3) where the symptoms were for three years those of a chronic peptic ulcer. Similar symptoms may occur in the intestine, a good example of sudden massive bleeding being that of Smith (1937). Hæmorrhage into the peritoneal cavity is much less common and usually such cases present as an acute emergency, exemplified by our *Case* 2, where bleeding followed degeneration of the centre of the tumour and perforation of the serosa. A similar case was reported by Millar (1928). The patient may first complain of an abdominal mass, which may reach a considerable size before being discovered. This history is not rare with extragastric tumours. Malignant cachexia is usually inconspicuous. Willenbacher (1928) reported a case causing pyloric obstruction be ball-valve action, and Barnett (1925) one in which there was gastroduodenal intussusception. In the intestine, apart from hæmorrhage, intussusception or varying degrees of obstruction are relatively common findings.

Moore (1927) gives the following as the principal radiological diagnostic criteria for intragastric smooth-muscle tumours: (1) A central or marginal filling defect, usually rounded and smooth, occasionally exhibiting a crater shadow in the dome. Manipulation in order to approximate the gastric walls is essential, especially for small tumours. Sometimes a pedicle, if present, may thus be outlined. (2) There is no contraction or spasm of the stomach. Peristalsis is usually uninterrupted and the gastric wall remains pliant. (3) Rugæ are not obliterated as in cancer, or thrown into convergent folds, as in ulcer. (4) Multiple growths are strongly indicative of benignity. Extragastric tumours manifest themselves by pressure or traction, thus producing a deformity which is likely to be misinterpreted as an ulcer or cancer.

TREATMENT

No form of radiotherapy has proved to produce any appreciable effect on these tumours, so that surgery is the treatment of choice. The procedure required must depend upon the extent of the tumour as found at operation, but since the majority are clearly delimited, the necessary margins of excision are much more easy to define than in the case of carcinomata, and consequently on many occasions less radical excision will suffice. Two of our cases (*Cases* 6, 7) appeared clinically inoperable. *Case* 1 required an extensive resection since it was an intragastric tumour situated high on the greater curvature, approaching the cardia closely and apparently infiltrating the splenic hilum. On the other hand, the pedunculated extragastric tumours were removed with only a narrow rim of stomach wall and no recurrence has yet made itself obvious, while histologically it appears that excision is complete in each instance. Thus it would seem that no set operation is to be preferred, as, for example, the radical subtotal gastrectomy recommended by Lahey and Colcock (1940).

Tumours of the duodenum are of necessity a very difficult surgical problem, and complete resection may be impossible, but *Case* 11 is included since it

presents therapeutic difficulties closely related to those of the leiomyomata, although histologically it is a hamartoma, or localized overgrowth of tissue elements normally present in this situation (Albrecht, 1904) consisting of smooth muscle and gland tubules resembling Brunner's glands. Such tumours, which are not neoplasms in the ordinary sense but rather developmental anomalies, are discussed in general by Nicholson (1921). No case exactly comparable with ours has been discovered in the literature.

In the small intestine local excision is often satisfactory, although nodules of tumour tissue may be missed. This is possible, however, even with extensive resection, and in view of the general low-grade malignancy it would seem best to rely on relatively local removal followed by careful post-operative supervision.

PROGNOSIS

Few of the papers on this subject give details of any extensive follow-up, but the reports as a whole suggest that, particularly where diagnosis is early, the outlook is very much better than with carcinomata of corresponding extent. Golden and Stout (1941) give the results of 30 clinically recognized cases, several of which had been observed for nearly ten years. In this series, which included a number of inoperable retroperitoneal tumours, 12 were living with no evidence of disease and 2 with such evidence, 9 died of the disease, there were 5 operative or early post-operative deaths, and 1 patient died of intercurrent disease, while no follow-up was available in 1 case.

FIG. 1.—*Case* 1. Pedunculated intragastric leiomyoma.

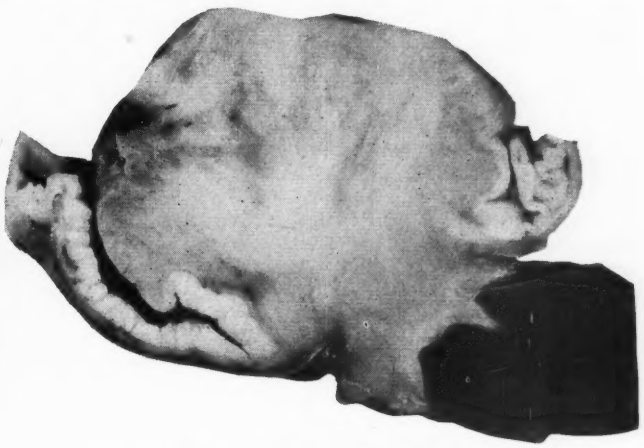

FIG. 2.—*Case* 1. The tumour bisected to show whorled surface, wide pedicle, and apparent infiltration of spleen.

CASE REPORTS

Case 1.—A man, aged 32 (Reg. No. 67887/47), was admitted on Jan. 20, 1947, complaining of listlessness and depression since November, 1945, which was six months after his release from a prisoner-of-war camp in Germany where he had spent five years. There had been anorexia for a month before admission. He said that in 1940 he had dysentery with blood and mucus in the stools, but had no specific treatment. After release from the prison camp he had a recurrence of similar complaints and received a course of emetine for suspected but unproven amœbiasis. He suffered from night sweats, occasional headaches, and backache. He also made much of several aggravating factors connected with his home life and work, and after thorough investigation which gave no indication of physical illness apart from an occasional rise of temperature in the evening to 99°–100° F., it was decided that his troubles might be accounted for by an anxiety state, and the assistance of a psychiatrist was sought. He was re-admitted on March 31, 1947, when there was noted to be a degree of hypochromic anæmia. A barium meal revealed a large filling defect at the cardiac end of the stomach, and there was much occult blood in the stools. The upper end of the stomach was explored by Mr. A. Elliot-Smith through an abdominothoracic approach. A mass was seen at the fundus apparently infiltrating the splenic hilum. A radical excision was performed in which the lower end of the œsophagus was divided, the upper half of the stomach and the spleen were removed in one block, and an anastomosis was performed with about 8 cm. of the stomach left in an intrathoracic position. Post-operatively, a little clear fluid was aspirated from the left pleural cavity on two occasions, but progress was good, and he was discharged on May 27, 1947. He appeared as an out-patient on Jan. 1, 1949, twenty months after operation, and was then feeling very well.

THE SPECIMEN (RISH 1340/47).—This consisted of the lower end of the œsophagus, cardia and fundal portion of stomach, and spleen. There was a rounded mass $8 \times 7{\cdot}5 \times 3$ cm. arising by a broad base from the upper end of the greater curvature and posterior wall of the stomach and projecting into the lumen, where it came very close to and appeared to obstruct the cardia. The surface was smooth, with slight nodularity. The mucosa all around the tumour appeared natural. The spleen was densely adherent (*Fig.* 1). On bisection (*Fig.* 2), the cut surface was seen to be uniformly firm, with whorled markings. Near the base it was covered by stomach mucosa for a distance of some 2 cm. Microscopically, the appearances differ little from place to place, and very little degeneration is seen. Bundles of smooth muscle-fibres lie in whorled arrangement and mitoses are rare. In a few areas the pattern is less well defined and there are large cells with hyperchromatic nuclei. Vascularity is moderate, and there is some diffuse round-cell infiltration. There is little evidence of encapsulation. Over the greater part of the surface the mucosa is eroded, and the tumour covered by a narrow necrotic layer. At the margins it is covered by gastric mucosa and muscularis mucosæ, the tumour mass coming up into the submucosa and spreading laterally for some distance between the muscle bundles of the main muscular coats, which are interrupted (*Fig.* 3). The outer aspect of the tumour is covered by serosa. The neoplasm is firmly attached to the spleen by dense fibrotic tissue, but

no infiltration is seen. It appears that excision is complete. On histological grounds this tumour did not show evidence of malignancy unless its lack of encapsulation and tendency to lateral spread be considered as such,

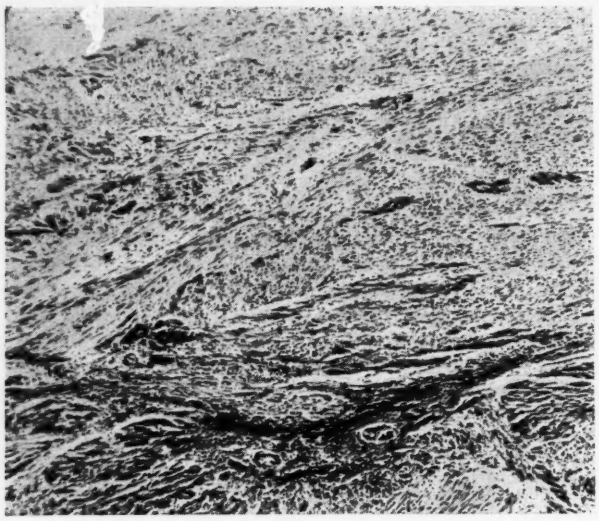

FIG. 3.—*Case* 1. Leiomyoma spreading laterally between muscle bundles. Hæmatoxylin and eosin. (× 42.)

and these appearances have been found almost constantly in smooth-muscle tumours.

Case 2.—A man, aged 51 (Reg. No. 81969/48), was admitted on Jan. 12, 1948. For about two weeks before admission he had noticed a lump in the abdomen and slight indigestion. Eight hours before admission there was a sudden onset of severe generalized abdominal pain,

FIG. 4.—*Case* 2. Extragastric leiomyosarcoma showing central pit in excised portion of gastric mucosa.

with pain also in the right scapular region. On examination, there was abdominal rigidity but the liver dullness was not diminished. It appeared likely that there was a perforated peptic ulcer, in spite of the atypical history and signs, and a temperature of 101° F. When under anæsthesia, a large mass could be felt in the right side of the abdomen. A laparotomy was performed, and a large quantity of blood-stained fluid was evacuated from the peritoneal cavity. A pedunculated tumour was found suspended from the lesser curvature of the stomach some 2·5 cm. above the pylorus. The tumour had burst at its distal end and discharged necrotic material and blood-clot. It was excised with a margin of apparently normal stomach wall around the pedicle. Post-operative progress was very good, and he was discharged for convalescence on Jan. 23, 1948. He was seen subsequently as

FIG. 5.—*Case* 2. The tumour bisected to show track through its centre passing from stomach to rupture into peritoneal cavity.

an out-patient. Until March, 1948, he complained of vague indigestion and slight dragging pain in the abdomen. A barium meal on March 13, 1948, showed a localized slight deformity with interruption of peristalsis in the lower third of the stomach. He was last seen on Jan. 1, 1949, when he was free of symptoms and appeared to be in very good health.

THE SPECIMEN.—The tumour (RISH 159/48) consisted of an ovoid mass 17·5 × 15 × 9 cm. almost entirely covered by peritoneum (*Figs.* 4, 5). It was attached to an ellipse of gastric wall by a short wide pedicle from one of its smallest sides. At the centre of the portion of mucosa there was a depression or evagination, at the middle of which commenced a channel which ran right through the necrotic centre of the tumour and continued as far as a rupture into the peritoneal cavity at the opposite end, 6 cm. long and 4 cm. wide. The tumour was dark red, with many large vessels. On the peritoneal aspect there was loss of sheen, and several fibrous adhesions were present. Microscopically the evagination is lined by epithelium similar to that of the surrounding gastric mucosa. In the submucosa there is dense infiltration by lymphocytes, plasma cells, and eosinophil leucocytes. In the depths of the evagination the mucosa becomes atrophic, and more deeply still it ceases. After this, the track through the tumour is lined by necrotic tissue with dense polymorphonuclear infiltration. The tumour mass appears to arise in the muscular coats of the stomach. It is of typical leiomyomatous structure, with numerous large spindle-shaped cells having nuclei with a well-defined nuclear membrane and fine chromatin net. Mitoses are not very numerous. Some parts of the specimen are cellular, while in others there is much interstitial hyaline, granular, or vacuolated acidophil material. There are many thin-walled widely dilated vascular spaces. Surrounding the specimen is

a serosal layer beneath which are stretched and flattened muscular layers. The appearances are those of a well-differentiated leiomyosarcoma.

Case 3.—An electrical engineer, aged 46 (Reg. No. 51432/45), was admitted on Dec. 19, 1945, having had attacks of peri-umbilical pain since 1941. They were present for one or two weeks, then absent for rather longer than this. They occurred two or three hours after meals

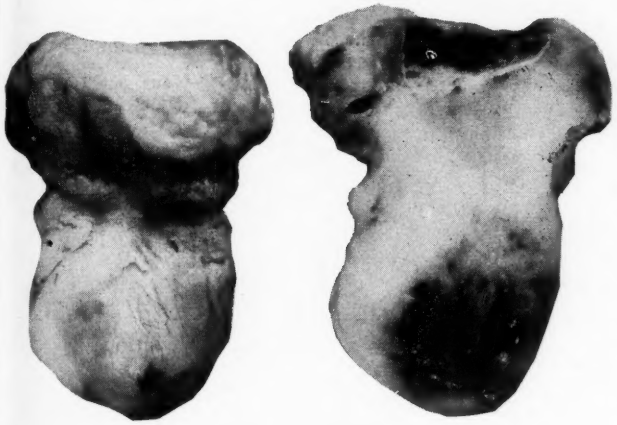

FIG. 6.—*Case* 3. Outer aspect and cut surface of extragastric leiomyoma to show deep ulceration of mucosa.

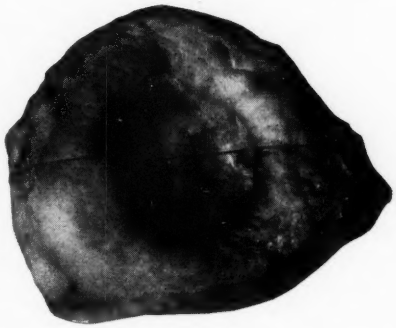

FIG. 7.—*Case* 3. Inner aspect of the tumour, showing close resemblance to a chronic peptic ulcer.

and were most easily relieved by a hot drink. A fortnight before admission the pain became much more severe than previously, and five days before admission it became almost continuous. At this time he was woken at night by the pain, and suffered occasionally from waterbrash. On examination, he was a well-built man, and no abnormal physical signs were found. A barium meal revealed a large gastric ulcer on the lesser curvature. A moderate amount of occult blood was found in one out of six specimens of fæces. He was treated conservatively, and on diet he became free of symptoms both in hospital and for six months after his discharge. However, in about June, 1946, the attacks recurred, particularly on occasions of dietary indiscretion. The site of pain was then slightly to the right of the midline and about 3 cm. below the umbilicus. In November, 1948, the pain became almost continuous, and he was re-admitted. After investigation, an exploratory laparotomy was performed by Mr. D. C. Corry on Nov. 13, 1948, and a rounded tumour with a smooth surface was seen projecting from a point near the centre of the lesser curvature of the stomach. This tumour (*Figs.* 6, 7) was excised with a surrounding rim of gastric mucosa. Subsequent progress was good, and no further symptoms had occurred up to the last time the patient was seen, in March, 1949.

THE SPECIMEN (RISH 4865/48).—This consisted of a firm subserosal tumour of bulbous shape, narrowing slightly towards the inner end, where it was surrounded by a cuff of stomach wall 4·5 cm. in diameter. The length of the tumour was 5 cm. and its greatest diameter 3 cm. Numerous large vessels were seen beneath the serosa, which was smooth and glistening. The mucosa at the base contained a central ulcer 2 cm. in diameter and of maximum depth 1 cm., with slightly overhanging edges. Microscopically, the gastric mucosa is intact on either side of the ulcer, where it is replaced by a necrotic layer beneath which is granulation tissue. More deeply there is a transition to the tumour itself, which consists of well-differentiated leiomyomatous tissue. This lies outside the muscularis mucosæ except at the ulcer site, where it comes to lie immediately below the granulating base, the muscularis mucosæ having disappeared. The main muscle coats of the stomach lie between the tumour and the serosa. Lateral spread is not seen and it appears that excision was complete.

Case 4.—A man, aged 57, was admitted to the Horton General Hospital, Banbury, in May, 1948, under the care of Mr. Lenton. He had had mild indigestion for a number of years, but said that he had never really been bothered by it. On admission, his complaints were of shortness of breath, chronic cough, occasional vomiting, and melæna. His hæmoglobin was 7·3 g. per 100 ml., and treatment at this time included transfusion. After discharge he was seen several times as an out-patient. In June, 1948, a barium meal showed an area of spasm in the central part of the stomach, which was presumed to be associated with an ulcer, although no crater was seen.

FIG. 8.—*Case* 4. Cut surface of extragastric leiomyosarcoma showing central degeneration. The wall was very thin in the lower part, but the apparent rupture is an artefact.

There were two further attacks of melæna during 1948, and on Jan. 22, 1949, an abdominal mass was felt. A laparotomy revealed a large, smooth, rounded tumour attached to the stomach wall near the lesser curvature by a short, wide pedicle. The tumour was removed with a surrounding rim of gastric mucosa. His convalescence up to March, 1949, was uneventful.

THE SPECIMEN (RISH 749/49).—This consisted of an almost smooth flattened ovoid subserosal tumour 13 × 12 × 6 cm. Attached to one end was a portion

of gastric mucosa 4 × 3 cm., which appeared intact. On bisection (*Fig.* 8) it was seen that there was a wall 2·5 to 4 cm. thick, with a central cavity 8 × 5 × 3·5 cm., containing blood and lined by fibrinous material. The tumour substance had a gelatinous greyish appearance with a tendency to radial striation. Microscopically, the gastric mucosa is intact, with a rather thick muscularis mucosæ. The tumour, which is of smooth-muscle type, appears to abut on the major muscular coats, but it is surrounded by condensed fibrous tissue, and there is compression but no visible infiltration of the muscularis. The degree of differentiation of the tumour varies greatly from place to place (*Fig.* 9). In some areas groups of

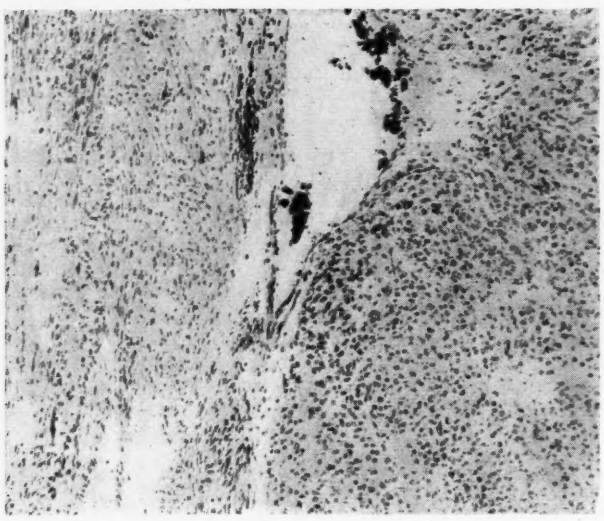

FIG. 9.—*Case* 4. Leiomyosarcoma showing adjoining areas of widely varying differentiation. On the left the pattern is well maintained, while on the right is a poorly-differentiated area. (× 42.)

typical, smooth-muscle cells are seen, with regimentation of nuclei and a considerable amount of interstitial fibrous tissue. In closely adjacent zones the histological appearances are those of a sarcoma, with a large proportion of ovoid and spheroidal cells and not infrequent mitoses. Here stroma is more scanty, and there are numerous areas of degeneration, which are in some places so arranged that the remaining tumour cells exhibit a pseudo-rosette formation around blood-vessels. Removal appears complete, but histologically this falls into the malignant group.

Case 5.—A girl of 19 (Reg. No. 59548/46) was admitted on July 7, 1946. In 1942 she had been confined to bed for some days with severe abdominal pain associated with backache and vomiting. This was attributed at the time to "kidney trouble" and resolved completely. In January, 1944, she had had a further attack of generalized abdominal pain, throbbing in character and accompanied by vomiting. She remained in bed for two weeks. Again she became well, and had no further trouble until the day before admission, when she developed similar pain. On the morning of admission she vomited, but there was no bowel irregularity. On examination, she looked feverish, with a temperature of 101·4° F. and pulse 124 per minute. There was generalized lower abdominal resistance, with tenderness in both inguinal regions. Rectal examination revealed general tenderness but no mass was felt. On the basis of a provisional diagnosis of pelvic peritonitis, the abdomen was opened by a paramedian incision. The presence of peritonitis was confirmed, and a tumour of the jejunum was found. A portion of jejunum including the tumour was excised and an anastomosis performed. Immediate recovery from the operation was satisfactory, but a residual abscess formed in the left iliac fossa. This was drained on Aug. 26. She was discharged fit on Sept. 18, and was very well with no evidence of recurrence in June, 1949.

THE SPECIMEN (RISH 2011/46).—This consisted of a portion of small intestine 10 cm. in length and 3 cm. in diameter, with a nodular, irregular, plum-coloured tumour approximately 5 × 5 × 4 cm. attached opposite the mesenteric border. On opening the jejunum, there

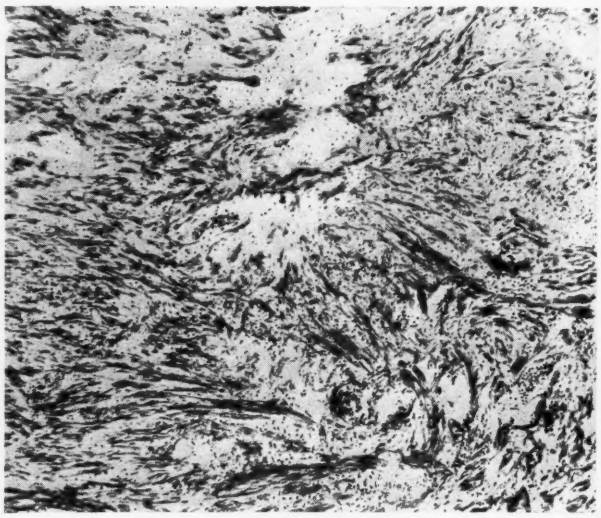

FIG. 10.—*Case* 5. Well-differentiated area in leiomyosarcoma. (× 42.)

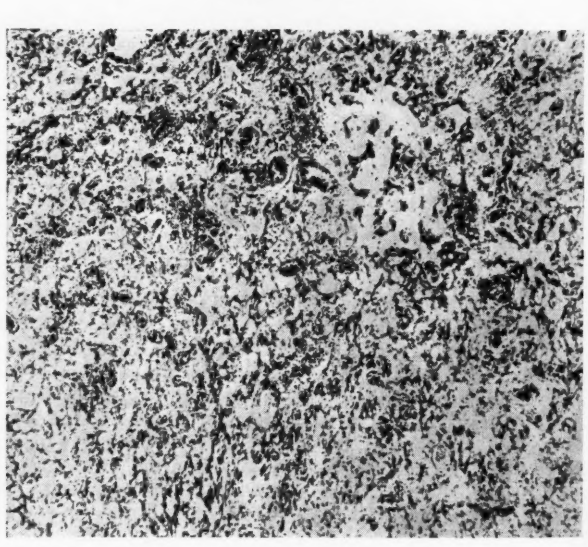

FIG. 11.—*Case* 5. Poorly-differentiated area with symplasmic masses in leiomyosarcoma. (× 42.)

was a depression 1 × 0·5 cm. in the mucous membrane at the site of attachment of the growth and extending to a depth of 0·5 cm. The outer surface was covered by serosa and there was no gross evidence of perforation. The cut surface showed a lobulated appearance, most of the nodules having a greyish-white centre while one was gelatinous and another cystic and filled with blood-clot. The tumour was attached to the intestine by a wide cone-shaped pedicle of fibrotic tissue passing 1·5 cm. down towards its centre. In one direction the submucosa appeared infiltrated for a distance of 2·5 cm. Microscopically, the mucosa is not invaded by the tumour, but is ulcerated over the area corresponding to the depression, and here the lining is of granulation tissue

rich in plasma cells. The tumour is of smooth-muscle type, with very considerable cellular variability. In some areas there are well-differentiated smooth-muscle cells, while elsewhere differentiation is poor and there is an increase in fibrous stroma and vascularity. In one place symplasmic areas of tumour cells are seen (*Figs.* 10, 11). The peritoneal surface is congested and covered by a fibrinopurulent exudate. While the main mass is subserous, in a small central area it passes inwards as far as the muscularis mucosæ. In view of the poorly differentiated areas this was considered to be a leiomyosarcoma, and it was thought likely that there might be microscopic perforation to account for the operative findings of peritonitis.

Case 6.—A retired postman, aged 77 (Reg. No. 60872/46), was admitted on Aug. 7, 1946, having noticed increasing weakness, pallor, and fatigue for about a year. Since May, 1946, these symptoms were severe. In July, 1946, his appetite progressively declined, so that by the time of admission there was profound anorexia. At this time there was pain across the lower part of the chest, coming on within a few minutes of taking food, and lasting about an hour. For a few days parasthesiæ of the hands had been noticed. On examination, the patient was a somewhat garrulous old man, easily rendered breathless by the effort of sitting up in bed, and extremely pale. A large mass was felt in the left hypochondrium with a definite edge extending from the left costal margin across the epigastrium. The hæmoglobin was 3·2 g./100 ml., erythrocytes 2,040,000 per c.mm., and blood-urea 60 mg./100 ml. Occult blood was present in large amounts in the fæces. A radiograph of the chest revealed fairly uniform opacity of the left lung field. With a barium meal, a constant gross deformity was found at the fundus of the stomach, suggestive of neoplasm. After transfusion the hæmoglobin rose to 7·3 g./100 ml., but it appeared that the tumour was inoperable and deterioration was observed. There was some consolidation at the base of the left lung, with low fever which subsided after sulphonamide therapy. The abdominal mass increased in size, although evidence of metastases did not appear and neither was there ascites. Death occurred on Jan. 20, 1947.

POST-MORTEM EXAMINATION (RIPM 42/47).—The body was that of an old man with extreme wasting and pallor. The left lung was uniformly solid and of mottled greyish appearance, resembling lobar pneumonia in the stage of grey hepatization, and weighing 1235 g. The right lung showed slight congestive changes only. There was a bilateral pleural effusion of clear, yellowish fluid, greater on the left, where it was loculated by adhesions which were easily broken down. The heart showed dilatation of all chambers, and the myocardium was thin and pale. There was some old nodularity of the mitral valve. The coronary arteries and aorta showed severe atheroma, with many calcified plaques, but the coronary vessels were patent. There was some increase in pericardial fluid. In the stomach there was a large tumour arising in the region of the greater curvature and spreading from the fundus to within 6 cm. of the pylorus. It was largely extragastric, with a smooth though coarsely lobulated outer surface. At the fundus there was ulceration through the mucosa to form three deep ulcers each about 3 cm. diameter with extensive basal necrosis and sloughing. There were dense adhesions to the spleen, which showed much old perisplenitis, and to the pancreas and transverse colon. The overall dimensions of the tumour mass were 20 × 10 × 9 cm. and it was of soft consistency and greyish in colour. No evidence of metastatic deposits was found. There was severe atheroma of the renal arteries, and both kidneys contained areas of coarse scarring. Microscopically, the tumour consists largely of fairly well-differentiated leiomyomatous tissue, but in some more vascular areas there are a proportion of ovoid and polyhedral cells. Mitoses are scanty, and in spite of a limited degree of marginal invasion it has only been after some doubt that this tumour has been assigned to the malignant group. Attachment to neighbouring organs appears to be by fibrous tissue without evidence of neoplastic involvement.

Case 7.—An apprentice boat builder, aged 19 (Reg. No. 13340/43), was admitted on July 28, 1943. His symptoms were dated from a cold in February, 1943, after which he had felt "run down", and within a few weeks had become very tired and breathless on exertion. He was admitted first to another hospital, where it was noted that his hæmoglobin was 6·1 g./100 ml., and traces

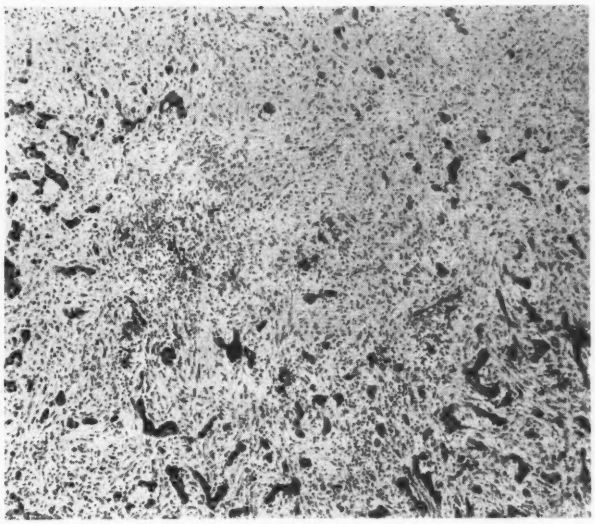

FIG. 12.—*Case* 7. Apparently very well differentiated hepatic metastasis. (× 42.)

of occult blood were found in the fæces. After transfusion his hæmoglobin rose to 8·7 g./100 ml. On July 21 he developed a sharp stabbing pain over the manubrium sterni with a non-productive cough, and his voice became hoarse.

On examination, he was a thin, pale boy, looking much younger than his age. The testes were very small. His blood-picture on admission showed hæmoglobin 5·2 g./100 ml.; erythrocytes 1,950,000 per c.mm.; leucocytes 8,300 per c.mm.; and reticulocytes 9 per cent. In the fæces were large quantities of occult blood. Routine physical examination did not reveal the cause of his anæmia, but a barium meal showed that there was "a soft polypoidal thickening at the fundus of the stomach". Radiographs of the long bones and chest showed no evidence of metastases. Shortly after admission he passed a melæna stool.

After transfusion, an exploratory laparotomy was performed by Mr. E. C. Bevers. There was a mass of extremely firm consistency and irregular nodular external surface 7·5 × 5 cm. at the fundus of the stomach, with firm attachment to the posterior abdominal wall and to the region of the left kidney. The para-aortic lymph-nodes were enlarged. It appeared that the condition was inoperable, and the abdomen was closed. Recovery from the operation was satisfactory, but the anæmia persisted, and death occurred on Dec. 5.

POST-MORTEM EXAMINATION.—This was performed at another hospital and only the abdominal organs were available for examination. At the fundus of the stomach, involving principally the posterior wall, was a firm tumour, 7 cm. diameter, firmly adherent to the pancreas and splenic pedicle. The tumour was partly intragastric, where it presented an ulcerated papilliferous appearance, and partly extragastric, where the surface was smooth

and nodular with surrounding adhesions. The regional lymph-nodes were enlarged. The liver was very pale, with numerous, discrete, round, white, secondary deposits up to 1·5 cm. diameter. Microscopically (RIPM 522/43), both primary tumour and hepatic metastases (*Fig.* 12) appear relatively well differentiated, mitoses are very few, and only on account of the presence of metastases can this tumour be definitely assigned to the malignant group. No evidence of neoplastic involvement of the lymph-nodes was found.

Case 8.—A housewife, aged 46 (Reg. No. 3175/43), was admitted on Jan. 11, 1944, having for eight years, since 1936, had intermittent burning epigastric pain not related to food. For a year before admission she had felt weak and noticed pallor. In May, 1943, there were more severe attacks of epigastric pain and she passed occasional tarry stools. On Sept. 27 she had a sudden attack of pain in the back of the head and neck, she felt cold, and the voices of other people became distant. She retired to bed, where she had bouts of vomiting for two days and a severe headache for a fortnight. When she tried to get up after this, she fainted, and passed very dark motions during the next two days. She was in bed altogether for five weeks.

On Nov. 22 she was seen as an out-patient, with epigastric tenderness but no palpable mass. There was enlargement of the heart to the left, and an apical systolic murmur was heard. The blood-pressure was 240/150 mm. Hg. There was slight weakness of all movements in the left arm. A barium meal showed an ulcer crater on the posterior wall of the body of the stomach with considerable rigidity around it, and it was thought that the findings were suspicious of a neoplasm. For a fortnight before admission she had a severe pain above the umbilicus coming on immediately after food, lasting about one hour and partially relieved by alkalis. On the day of admission there was a hæmatemesis of some 600 ml. of dark blood. At the time of admission the patient was obviously seriously ill, and full examination was deferred. There was slight tenderness just above the umbilicus in the midline. The blood-pressure was 170/110 mm. Hg, and the hæmoglobin 8·4 gm./100 ml. Treatment was conservative, with Sippy II diet. On Jan. 12, 1944, the day following admission, there was a further hæmatemesis of about 900 ml., and a transfusion of 1600 ml. of blood was given. From then on progress appeared satisfactory, although there were still occasional attacks of epigastric pain. On Feb. 10, just after being washed, she complained of feeling " faint and queer in the head ". She then fell back pulseless, with stertorous breathing, and died within two minutes.

POST-MORTEM EXAMINATION (RIPM 75/44).—The body was seen to be that of a pale, normally developed woman of middle age. The heart weighed 415 g., with moderate left ventricular hypertrophy. There was atheroma of the coronary arteries. Along the lesser curvature of the stomach lay a pedunculated, submucosal, roughly cylindrical tumour mass 7 × 4 × 3 cm., with its long axis parallel to that of the stomach. The tumour was for the most part covered by gastric mucosa. However, in the middle of its anterior surface there was a punched-out ulcer 0·6 cm. diameter and 1 cm. deep, and towards the distal end was a second shallower ulcer 1·5 cm. diameter. The peritoneal surface of the stomach over the tumour did not appear to be affected. The colon contained tarry fæces. Both kidneys had fine scarring of the surface. The capsules stripped easily, the cortex was not reduced, and cortico-medullary demarcation was good. The arcuate vessels were prominent. There was extensive subarachnoid hæmorrhage over the base of the brain, arising from a ruptured aneurysm 0·5 cm. diameter on the anterior communicating artery. The meninges showed brownish-yellow pigmentation suggestive of previous hæmorrhage. There was a meningioma in the right parietal region producing a cavity in the right cerebral hemisphere 1·5 cm. diameter. No evidence of metastases from the gastric tumour was found. Microscopically, the gastric tumour appeared to have a well-differentiated form throughout. The ulcers had a necrotic base beneath which was granulation tissue with dense polymorphonuclear and round-cell infiltration. Histologically this tumour falls into the benign group.

Case 9.—A man of 40 (Reg. No. 87580/48) was admitted on June 9, 1948, on account of recurrent attacks of abdominal pain, mainly in the right iliac fossa. An appendicectomy was performed, but post-operatively paralytic ileus developed. Re-exploration revealed no organic obstruction, but death occurred the day after this.

At the post-mortem examination (RIPM 271/48), a greatly dilated small intestine was found. Also, incidentally, there was a small submucosal mass on the lesser curvature of the stomach 3 cm. from the pylorus. This swelling, 1·3 × 0·8 cm., was connected by a short pedicle with an extragastric tumour 2·3 × 2 × 1 cm. lying along the serosa of the lesser curvature. Histologically, the tumour is a typical well-differentiated leiomyoma.

Case 10.—A labourer, aged 67 (Reg. No. 101371/49), was admitted on Feb. 27, 1949, having been well until a month before admission, when he developed attacks of epigastric pain apparently unrelated to food. This pain was said to move from side to side, and sometimes to go through to the back, and it kept him awake at night. The day before admission he had a hæmatemesis, and he vomited more blood and passed a melæna stool early on the day of admission. On examination, he was severely exsanguinated, and transfusion was started. He was given citrated milk and water by mouth. The following day auricular fibrillation was observed, it was evident that hæmorrhage was continuing, and on March 1 he died.

At the post-mortem examination (RIPM 120/49) the stomach was found to be greatly distended and to contain 850 ml. of coagulated blood. At the centre of the lesser curvature was a peptic ulcer 3·2 × 2·3 cm., from the middle of which protruded an eroded atheromatous artery 0·4 cm. diameter which was clearly the source of hæmorrhage. An incidental finding was a smooth tumour in the posterior wall of the stomach 5 cm. above the pylorus. The tumour was 4·5 cm. in diameter and 1·5 cm. in thickness, and both mucosa and serosa appeared to move freely over it. Histologically, this was a typical leiomyoma.

Case 11.—A girl, aged 8 months (Reg. No. 68752/47), was admitted on Feb. 24, 1947. No abnormality was noted during pregnancy or delivery. There had been occasional slight vomiting, always stained with brownish material, ever since birth. For three weeks the vomiting had been severe, the stools very dark, and pallor had developed. On examination, a well-developed but extremely pale child was seen, with slightly indrawn fontanelle. No abdominal tenderness or mass was found. The hæmoglobin was 4·1 g./100 ml., erythrocytes 1,900,000 per c.mm., and reticulocytes 7·5 per cent. After transfusion, further investigations were undertaken, revealing occult blood in all specimens of fæces, and also in the fasting gastric juice. A barium meal showed an atonic stomach and first part of duodenum, with deformity and partial obstruction of the second part. The parents would not allow laparotomy at this stage, but a hæmatemesis on April 3 caused them to consent, and at operation on April 7 Mr. A. S. Till performed subtotal removal of a polypoid mass from the posterior wall of the second part of the duodenum, extending down to the upper end of the jejunum. Further transfusions were undertaken, and on April 23 the child was discharged home well, with good colour, hæmoglobin 13·5 g./100 ml., feeding satisfactorily, and with no vomiting or fæcal occult blood. Vomiting recurred early in July, and the girl

was re-admitted on July 29 of good colour but fretful and with poor muscle tone. A barium meal showed extreme narrowing of the third part of the duodenum. Vomiting continued, and on Aug. 7 a gastro-enterostomy was performed. On Aug. 17 two large melæna stools

FIG. 13.—*Case* 11. Hamartoma (adenoleiomyoma) of duodenum.

were passed, and there was a sharp drop in the hæmoglobin level. Again transfusion was carried out, and the next day, when it was found that the stoma was satisfactory, the remnant of the tumour was removed. The post-operative course was good, and inquiry in May, 1949, has revealed that subsequent progress has been excellent, with no recurrence of symptoms.

The first specimen (RISH 1143/47) (*Fig.* 13) was a polypoid mass consisting of numerous rounded nodules, 6·5 × 3 × 3 cm. weighing 42·5 g. The second (RISH 2897/47) was similar, 5 × 4·5 × 3·5 cm. weighing 28 g.

FIG. 14.—*Case* 11. Glandular area in adenoleiomyoma, with central dilated ducts and surrounding smooth-muscle tissue. (× 42.)

The individual nodules varied from 2·5 to 0·2 cm. in diameter, averaging 0·5 cm. Histologically the two are identical. The tissue consists of proliferated glandular and smooth-muscle elements (*Fig.* 14). The glands are of Brunner type, and tend to be collected in masses surrounded by muscular tissue with central dilated ducts. The ducts contain numerous goblet cells, and in some places mucoid material has permeated the interstitial tissue in their neighbourhood. The muscular as well as the glandular elements appear everywhere perfectly differentiated, and this tumour is regarded as a hamartoma.

SUMMARY

Ten cases of smooth-muscle tumours of the gastro-intestinal tract are reported, with, in addition, an adenoleiomyomatous hamartoma of the duodenum.

Their relatively good prognosis compared with carcinomata is emphasized.

I wish to express my thanks to Dr. A. H. T. Robb-Smith for his encouragement and criticism; to members of the staff of the Radcliffe Infirmary who have allowed me to use their case records; and to Dr. G. A. C. Summers for assistance with photography.

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SUCCESSFUL RESECTION OF A LARGE CAVERNOUS LYMPHANGIOMATOID LESION OF THE LIVER OF A CHILD AGED 19 MONTHS

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PRIMARY liver tumours in children are rare, and their successful excision has not often been reported. Recent accounts of the successful removal of such tumours include reports of resection of hepatomata by Duckett and Montgomery (1947), of hamartomata by Ladd and Gross (1941) and by Benson and Penberthy (1942), and of a tumour described by Donovan and Santulli (1946) as a mesenchymoma. There are many accounts of excision of hepatic hæmangiomata in the literature, but the youngest patient in a series of 67 cases reviewed by Shumacker (1942) was 6 years old.

The following account is of a case of resection of a large cystic mass from the liver of a child aged 19 months. Although the nature of the lesion in this case remains uncertain, clinically and at operation the problem which it presented did not differ essentially from that occurring in cases of hamartomata and of true tumours such as those mentioned above.

CASE REPORT

HISTORY.—G. W. (Radcliffe Infirmary No. 85477/48), a boy 19 months old, was admitted to the Radcliffe Infirmary with abdominal distension in April, 1948, under the care of Dr. Victoria Smallpeice. He was a first-born child, delivered spontaneously at full-term after a normal pregnancy. His birth-weight was 3·7 kg. He progressed well on breast-feeding, was weaned during the seventh month, and walked soon after his first birthday anniversary.

In January, 1948, when 15 months old, he was in bed for a fortnight with bronchitis. Soon after, his abdomen was noticed to be swollen. The degree of distension increased, and later the child appeared to have pain in the abdomen and in the legs. He became irritable and lost his appetite. There was no bowel or urinary disorder. The family history gave no relevant information.

ON EXAMINATION.—He was a thin boy, weighing 13·3 kg. His abdomen was greatly distended, measuring 70 cm. in circumference. It was almost completely filled by a large tumour, which, examined with the child under sedation, was found to extend from the right flank and from under the right costal margin to well down into the right iliac fossa and well over the midline. The rounded upper margin could be felt 5·5 cm. below the xiphisternum, and the lower margin 8 cm. above the pubis. The mass was dull to percussion and slightly mobile. It was firm in consistency, in parts apparently cystic, but harder towards the flank and at its left lower extremity. The superficial abdominal veins were dilated. No other abnormalities were found on clinical examination.

Hæmatological Examination.—Hæmoglobin 61 per cent.* Total leucocyte count 15,000 per c.mm.; differential count:—neutrophil polymorphonuclear leucocytes 43 per cent (6450 per c.mm.), lymphocytes 50 per cent (7500 per c.mm.), monocytes 7 per cent (1050 per c.mm.).

Blood-urea: 34 mg. per 100 ml.

Radiological Examination.—A large mass displaced the stomach and colon upwards and to the left. Intravenous pyelography: both kidneys secreted normally, but were displaced somewhat upwards.

A provisional diagnosis of intra-abdominal cyst, possibly retroperitoneal, was made.

FIRST OPERATION (Mr. A. Elliot-Smith).—On April 10, 1948, under gas, oxygen, and ether anæsthesia, by insufflation into a rubber face-piece, the abdomen was explored through a right upper transrectus incision. On opening the peritoneum an enormous, smooth, reddish tumour presented. It appeared to arise from the lower surface of the liver and to be divided into two lobules by a fibrous constricting band, thought at first to be the ligamentum teres, running over its antero-inferior surface. An attempt to tap the tumour in order to reduce its size was at first unsuccessful, but after initial failures a few ounces of yellow fluid were obtained. The tumour was partly solid, partly cystic, the wall of the cavity tapped being 1 cm. thick. The incision was prolonged and the mass delivered. The liver was stretched over the anterior surface of the mass and a plane of cleavage existed between them. The fibrous band mentioned above was divided, and separation proceeded until a pedicle-like structure measuring 3·7 × 7·5 cm. was defined near the hilum of the liver. The tumour was now excised with a surrounding margin of liver by sharp dissection. Multiple bleeding points were clamped, and hæmostasis was secured by catgut transfixion ligatures. The liver was reconstituted by several deep catgut mattress stitches, and the wound closed.

The gall-bladder could not be identified during the operation, but on examination of the specimen was found to lie beneath the fibrous band divided during removal of the tumour.

A blood transfusion of 540 ml. was started slowly before operation, and was followed by 1620 ml. of 2½ per cent glucose in 0·25 per cent saline. A penicillin course of 20,000 units 3-hourly was begun.

PROGRESS.—From the day following operation it became increasingly obvious that the child was suffering from obstructive jaundice. A course of synthetic vitamin K (tetrasodium 2-methyl-1: 4-naphthahydroquinone diphosphate), 10 mg. daily, total 50 mg., was given. His general condition deteriorated, and a further exploration was carried out.

SECOND OPERATION (Mr. A. Elliot-Smith).—On April 17, under gas, oxygen, and ether anæsthesia, the abdomen was reopened through the original incision. The liver was well healed, and surprisingly normal in appearance and contour. The deep catgut sutures in the region of the porta hepatis were seen, and three of them cut. A dilated duct was exposed. It contained bile on needling, and had been occluded by one of the deep catgut sutures. This stitch was removed. The wound was closed, with a separate stab drain.

A blood transfusion of 400 ml. was started during the operation and followed by glucose-saline. A sulphamezathine course of 0·25 g. 4-hourly, total 9 g., was given.

PROGRESS NOTES.—

April 18: Bile drainage from the tube.

April 19: Traces of bile in the stool.

April 20: Jaundice diminishing. Hæmatological examination: Hæmoglobin 41 per cent; reticulocytes

* The results of hæmoglobin estimations are quoted throughout in percentage, 100 per cent hæmoglobin being equivalent to 14·8 g. Hb per 100 ml. of blood.

2 per cent; total leucocyte count 6000 per c.mm.; prothrombin time 50 per cent of normal.

April 21: Normal stool. Blood transfusion of 200 ml.

April 22: Blood-urea 36 mg. per 100 ml. Plasma-bilirubin 8·75 mg. per 100 ml. Alkaline plasma-phosphatase 24 units per 100 ml. Serum-proteins 4·5 g. per 100 ml. (albumin 2·82 g., globulin 1·68 g.).

April 23: Blood transfusion of 120 ml.

April 24: Drainage tube removed. Prothrombin time normal.

April 28: General condition much improved. Liver function apparently within normal limits. Hæmatological

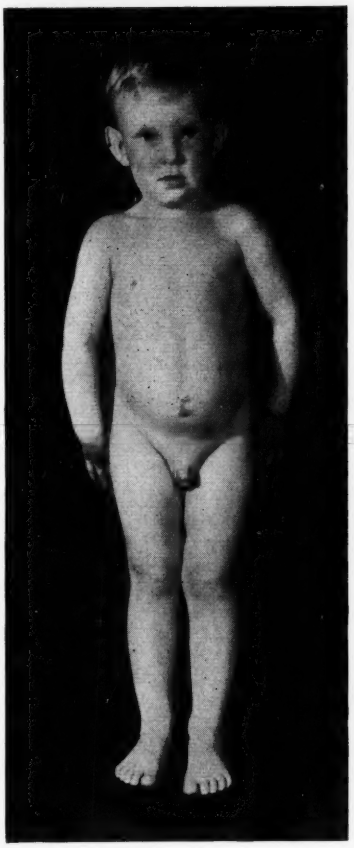

FIG. 15.—G. W., age 2 years 7 months, one year after operation.

examination: Hæmoglobin 57 per cent; reticulocytes 2·2 per cent. Blood-urea 28 mg. per 100 ml. Plasma-bilirubin 2·5 mg. per 100 ml. Alkaline plasma-phosphatase 32 units per 100 ml. Serum-proteins 6·5 g. per 100 ml. (albumin 4·4 g., globulin 2·1 g.).

April 30: Sutures removed. Wound healing, but with some infection by a *Proteus* organism. Penicillin stopped (total dose 3 million units).

Subsequent Progress.—From this time the child continued to make a slow and halting recovery, at first running a low-grade pyrexia. He was discharged to his home on May 19, and soon regained his previous happy disposition.

The photograph (*Fig.* 15) was taken a year later. When seen in April, 1950, two years after operation, he was well, weighed 16·2 kg., and there were no abnormal clinical findings. Laboratory investigations gave the following results—hæmoglobin 93 per cent, prothrombin time normal; blood urea 33 m.g. per 100 ml.; alkaline plasma-phosphatase 31 units per 100 ml.; plasma-proteins 6·4 g. per 100 ml. (albumin 4·4 g).

THE SPECIMEN (*Figs.* 16, 17).—In its general shape the specimen (2060 g., 21 × 18 × 8 cm.) resembled a liver. It had a complete covering of normal peritoneum, except for a rounded area, 9 cm. in diameter, at the middle of

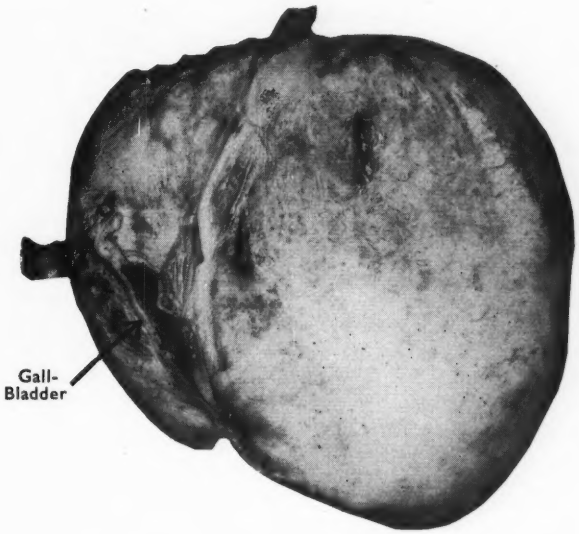

FIG. 16.—Photograph of specimen showing its antero-inferior surface. The gall-bladder has been laid open. (× ½.)

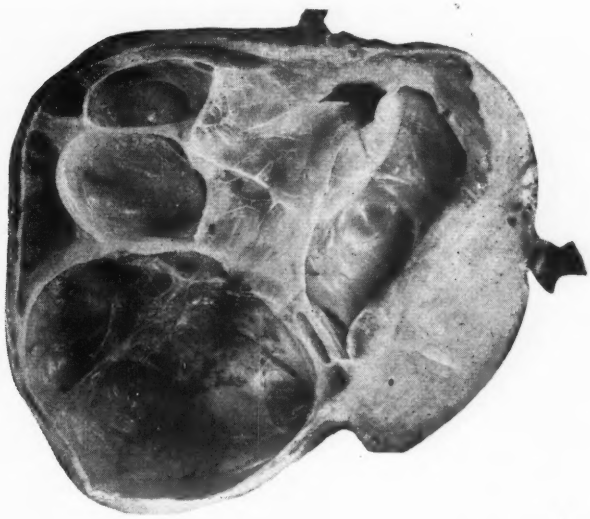

FIG. 17.—Photograph of anterior half of bisected specimen viewed from behind. At the right side is seen the solid mass of hepatic tissue adjacent to the plane of surgical dissection. (× ½.)

the anterosuperior surface; this area, representing the plane of the surgical dissection of the mass from the rest of the liver, was lobulated, and consisted of pale liver tissue, which appeared finely cirrhotic over the dissected surface although the serosal surface was quite smooth. The larger (antero-inferior) face of the mass was divided by a fibrous constriction into two areas, one 11 cm. across and the other 9 cm. In this fibrous band there was a duct-like structure, 9 cm. long by 0·5–0·7 cm. in diameter, blind at each end, but with a 2-mm. diameter opening in its wall 2 cm. from the upper end. The duct-like structure was shown histologically to be the gall-bladder, lined by atrophic bile-stained epithelium, and the opening

in its wall was presumably the upper extremity of the cystic duct, cut across at operation. Bisection of the specimen showed that the lobulated area of hepatic tissue extended inwards from the surface to a depth of 6 cm., and was continuous at its periphery with a firm fibrous wall, 0·7 to 1·5 cm. thick, which surrounded the main bulk of the tumour-like mass, and which was covered on its outer surface by peritoneum. The rounded tumour-like mass consisted of a series of cysts, from 2 cm.

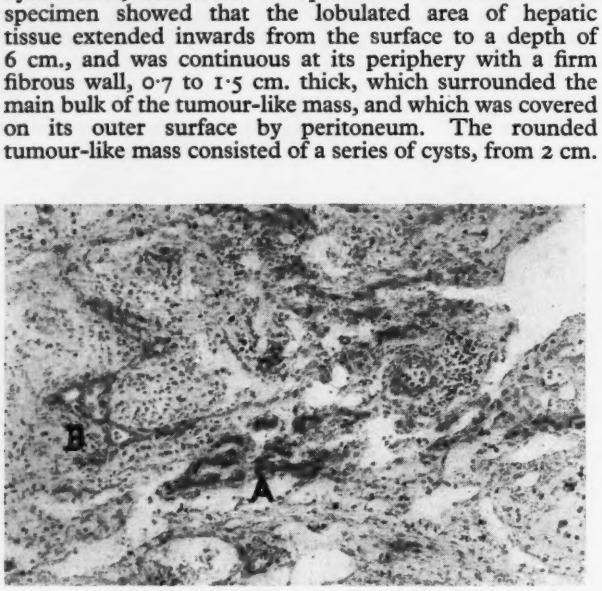

FIG. 18.—Photomicrograph of part of a section from anterior wall of cystic mass, showing surviving cords of liver cells with intervening sinusoids, and continuity between sinusoids and endothelium-lined spaces elsewhere in the field. A, group of liver cells with sinusoids; B, biliary ductules. Hæmatoxylin and eosin. (× 65.)

to 12 cm. in diameter, containing clear, pale yellow fluid or gelatinous material. Some cysts were traversed by scanty, fine, interlacing trabeculæ, while in others remnants of trabeculæ were indicated only by slightly raised ridges in the walls; the lining of still other cysts was completely smooth. The smallest cysts were those at the periphery

FIG. 20.—Photomicrograph of spongy inner zone of anterior wall of cystic mass, showing coarse meshwork of connective-tissue fibres, with great œdema. Trichrome stain. (× 59.)

of the mass, and they were partly filled by œdematous spongy tissue. Similar soft œdematous tissue separated the individual cysts, and formed a lining to the fibrous wall of the mass.

Histological Examination.—Sections were prepared from paraffin blocks of representative parts of the specimen after fixation in formol-saline (4 per cent formaldehyde), and were stained by: iron hæmatoxylin and eosin; Mallory's phosphotungstic acid hæmatoxylin; iron hæmatoxylin, Ponceau acid fuchsin and fast green; Robb-Smith's reticulin method; Weigert's elastic-tissue stain; Perls's reaction; and toluidine blue. Frozen sections were stained with Sudan IV and Sudan black.

Sections of the anterior wall of the cystic mass (*Figs.* 18, 19) show that it consists of a broad outer zone of loose-textured, cellular connective tissue, covered on its surface by serosa. Throughout this zone there are

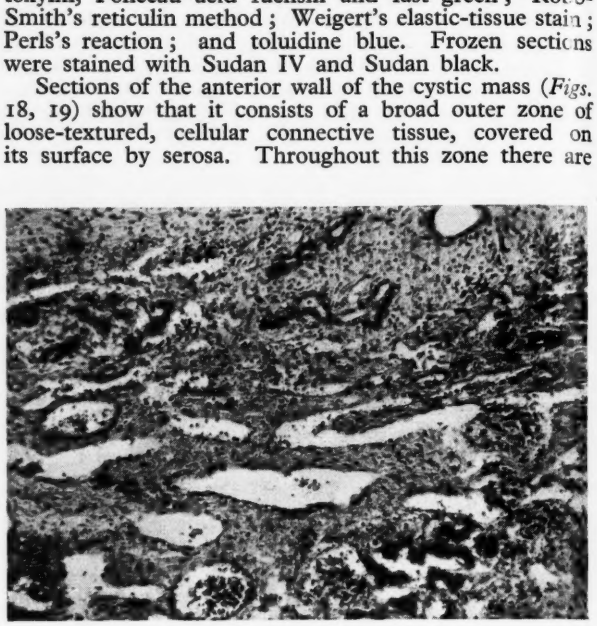

FIG. 19.—Photograph of another area from wall of cystic mass, showing a similar picture to that in *Fig.* 18. Phosphotungstic acid hæmatoxylin. (× 55.)

small groups of liver cells, the arrangement of which in cords is still maintained. These cords are separated by slightly dilated vascular channels, continuous with a series of much larger intercommunicating channels in the areas where the liver cells are absent; the architecture suggests that these channels are hepatic blood sinusoids which have dilated in association with atrophy of the liver parenchyma. Capillary bile-ducts are numerous in the outer zone, some of them considerably dilated; their epithelium is normal in appearance, or more often flattened, so that in some instances it is impossible to distinguish between vascular and biliary channels. These ductules are, in some places, in continuity with the cords of liver cells, but usually no such connexion is demonstrable; often the ductules are the only epithelial structures in a field. Many of them show outbudding of new biliary channels. Slight lymphocytic and plasma-cell infiltration of the tissues is seen, particularly near the ductules, and occasional eosinophil granulocytes and mast cells are present. Numerous small hæmorrhages are found near the dilated sinusoids, particularly where the parenchymatous cells have disappeared.

The spongy inner zone of the anterior wall of the mass (*Fig.* 20) is a coarse meshwork of scanty collagen and reticulin fibres, with a few fibroblasts and fibrocytes, occasional capillary blood-vessels, and a few small groups of larger vessels, arterioles and venules, the size, arrangement, and structure of which closely resemble those of vessels in portal tracts. No epithelial elements are seen in this zone. The interstices of the meshwork contain a partly granular, partly homogeneous, eosinophil substance, probably coagulated tissue fluid, scattered in which are occasional large vacuolated cells. In the paraffin sections the vacuolated cells resemble lipoblasts, but in frozen sections no fat was demonstrated in them, and it seems probable that they are histiocytes which have ingested material from the œdematous tissue; some of them contain finely dispersed minute granules in the cytoplasm which give a faintly positive reaction for iron. Numerous fine reticulin fibrils extend for a short distance from the reticulin framework into the tissue spaces.

The cystic spaces forming the central portion of the mass have no lining other than a slight condensation of the surrounding œdematous tissue, which at the surface of the walls of the cavities shows a narrow zone of permeation by fibrin.

Sections of the liver resected with the cystic mass (*Fig.* 21), and of a small biopsy specimen taken during the first operation from the liver adjacent to the mass, show much periportal fibrosis, with, in places, œdema

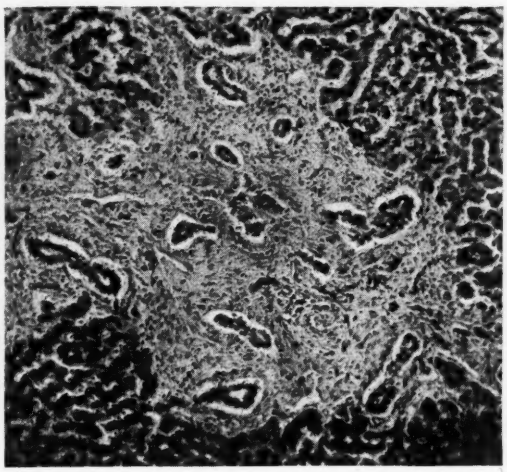

FIG. 21.—Photomicrograph of liver tissue adjacent to cystic mass, showing periportal fibrosis with increased number of bile-ducts. Trichrome stain. (× 55.)

of the fibrous tissue. The number of bile-ducts is considerably increased, and moderate mononuclear leucocytic infiltration and very occasional minute hæmopoietic foci are present. The lobular architecture of the liver is maintained, although distorted by the periportal fibrosis. The parenchymatous cells appear normal.

DISCUSSSION OF THE PATHOLOGICAL CHANGES

It does not seem possible to deduce from the pathological findings a completely satisfactory explanation of the nature of the cystic mass removed from the liver of this child.

Progressive increase of abdominal girth was the most striking feature of the short clinical history, which extended over only three months. This, together with the great size of the tumour found at operation, suggested that the condition would prove to be neoplastic. Examination of the bisected specimen showed that the mass was mainly cystic, with only a relatively narrow zone of solid tissue at its periphery, and on the general appearances a provisional diagnosis of 'lymphangioma' was made. The microscopical findings, however, do not appear fully to confirm the impression which was gained on macroscopic examination.

Study of histological preparations of representative parts of the specimen led to consideration of two possible processes by which the nature of the lesion might be explained. Firstly, it might be interpreted as tumour growth, either a true neoplasm or a hamartoma, with secondary degenerative changes. There is, however, no unequivocal evidence of tumour-like overgrowth of any tissue elements. The channels in the connective tissue of the peripheral zone of the mass appear for the most part to be dilated blood-sinuses, with a smaller proportion of dilated biliary ductules, although it is impossible to deny categorically that some may be lymphatic channels; were the majority lymphatic, a lymphangiomatous condition might be presumed, but proof of this would demand demonstration of a more striking lymphatic overgrowth than is in evidence. The lack of evident transitional stages in the development of the cystic spaces from the channels seems considerably to weaken the case for making a diagnosis of lymphangioma.

Secondly, the pathological findings might be interpreted as indicative of pseudocystic degeneration occurring in part of the liver, the parenchyma having undergone atrophy, with œdema and partial liquefaction of the stroma resulting in pseudocyst formation. Were this interpretation to be maintained, it would be necessary to find a convincing explanation of the apparent localization of such a process to a single part of the liver. In this respect, the marked periportal fibrosis in the adjoining liver tissue has occasioned some speculation concerning its possible relationship to the development of a pseudocystic degeneration limited to part of the liver. In this patient, the appearance of the rest of the liver at the first operation did not suggest the presence of cirrhosis or indeed of any pathological change other than the distortion due to the presence of the large mass which was excised. The normal appearance and restoration of contour of the liver in the period of seven days between the two operations suggests that the cirrhotic change may have involved only that part of the organ in the immediate vicinity of the resected mass, but they are by no means necessarily inconsistent with the presence of a generalized cirrhosis. If there were, in fact, only a localized cirrhosis, the reason for the localization remains obscure; congenital stricture of the bile-duct draining one segment of the liver is a possibility. So-called partial cirrhosis, i.e., cirrhosis involving only a part of the organ, has been described (Rössle, 1930), and could develop in association with stenosis of an intrahepatic bile-duct. In the present case, the atrophy and distortion of the gall-bladder may be attributed to pressure by the neighbouring mass in the liver, and there was nothing to suggest any congenital malformation of it, such as may accompany atresia of the right hepatic duct (Hanser, 1929).

It is possible that severe localized periportal fibrosis may have resulted in ischæmic atrophy of the parenchyma, due to vascular obstruction, œdema developing for the same reason. Widespread ischæmic atrophy of this degree is not, however, a feature of cirrhosis, nor is pseudocystic degeneration, although the fibrous tissue in cirrhosis may indeed be moderately œdematous, an occurrence which seems to be the result of the associated circulatory obstruction.

A diagnosis of congenital cystic liver of the usual types appears to be excluded by the localization of the changes, the structure of the walls of the cystic areas, and the relations of these to the surrounding tissues; no bile-duct dilatation of cystic dimensions was found, nor was any trace of a cellular lining to the cavities present.

In summary, it can be said, therefore, that it is possible that the lesion in this case is lymphangiomatous with secondary degenerative changes, but the evidence is unsatisfactory and neither a pathogenetic nor a complete morphological diagnosis is possible.

REVIEW OF AVAILABLE LITERATURE RELEVANT TO THE PRESENT PATHOLOGICAL PROBLEM

Only one record (Maresch, 1903) has been found in the literature of a case apparently identical with that here presented, but a case showing many points of similarity, and probably of the same nature, has recently been reported by Patton (1948).

The report by Maresch (1903) is a detailed account of the clinical and pathological findings in the case of a 5-year-old girl, whose history was of an increase in abdominal girth for three years, at first gradual but later rapid. Clinically, the child was emaciated and presented what was thought to be a large ovarian cyst. At operation, the tumour was found to arise from the right lobe of the liver, by a pedicle a handbreadth in width and fully two finger-breadths thick. The tumour was removed; severe hæmorrhage occurred from a tear in a wide thin-walled vein, but this was controlled. The child recovered from the operation, and was said to be in good health an unstated period after discharge from hospital. Maresch describes the tumour as having the shape of a flattened ball, its diameters 20 and 18 cm. and thickness 8 cm. His macroscopical description corresponds very closely in all details with that of our specimen, and this similarity is also remarkably close in the account of the histological findings. He concluded that his was a case of *lymphangioma of the liver*. This diagnosis appears to have been based mainly on his interpretation of the endothelium-lined spaces as being of lymphangiomatous nature, whereas in our case it has seemed more logical to consider them as hepatic sinusoids which have become dilated following disappearance of the parenchyma around them. His *Figure* 2 does not seem clearly to show the delimitation of the " cavernous or cystic tumour " from the surrounding liver parenchyma, such as he claims it to do, and to this alleged connective-tissue zone separating the two types of tissue (" lymphangiomatous " and hepatic) he attaches some weight in the development of his diagnosis of the neoplastic nature of the lesion. It seems beyond doubt that the condition described by Maresch and that present in the case of the patient studied by us are identical. In relation to the rapid growth of the lesion in our case, it is of interest to note that Maresch writes: " The recent rapid growth of the tumour indicated in the anamnesis is doubtless adequately explained by the abundant œdematous permeation of the relatively thin-stalked tumour "; he makes no further comment as to the mechanism by which the œdema developed.

The case reported by Patton (1948) is that of a girl, aged 16½ months, who was apparently in normal health until an abdominal mass was found two weeks prior to her admission to hospital. The condition was diagnosed as probably a mesenteric cyst, and she was operated upon six days after admission. A tumour, its base broadly incorporated into the right lobe of the liver and its medial border immediately adjacent to the gall-bladder, was found and resected, this necessitating removal of nearly half of the right lobe of the liver. She was discharged from hospital on the eleventh day after operation, and was in good health when seen five months later. The specimen is described as a heart-shaped mass, 17 × 17 × 9·5 cm., weighing 1575 g.; the illustrations and description indicate that it was mainly solid, but with several cysts, the largest 8 cm. in diameter. Patton records the pathological diagnosis as *hamartoma of the liver*. From the histological description the lesion in his case resembles ours quite closely. Pathologically, the main differences between the two cases seem to be the more solid structure of Patton's case and the absence of abnormality in the liver tissue at the proximal end of his specimen, although glandular structures, resembling bile-ducts " in a general way ", are described in the periportal connective tissue in the liver tissue adjacent to the tumour mass. It seems therefore probable that Patton's " hamartoma " is of the same nature as the condition present in our case, despite the unequivocal assertion that it is a hamartoma, an interpretation which may be open to debate.

Accounts of a number of other cases show some features of similarity to ours. In a recent paper concerning radiological diagnosis of primary tumours and of non-parasitic cysts of the liver in children, Stašek (1949) summarizes the case (*Case* 1 in his series) of a 19-month-old boy who clinically and at operation seems to have presented a picture essentially the same as that in our patient. Škorpil's microscopical report on the specimen in this case is quoted by Stašek; the tumour removed from the liver was a multicystic one, the cavities of which, unlike those in our case, are described as having an uncertain epithelial lining, but the cells could not be identified on account of degeneration. In other details also the microscopical appearances seem to have differed from those seen in our case. A developmental anomaly was suggested by Škorpil as the origin of the tumour. This case has apparently been described previously by Kafka (1946), but his paper is unfortunately not available to us for perusal, nor has it been possible to consult a number of other Czech papers referred to by Stašek as dealing with examples of primary liver tumours and non-parasitic cysts.

Baccarini (1936) reported a case of what he considered a congenital polycystic liver of hamartomatous nature; the patient was a 6-month-old girl. In his case the liver was more widely involved than in ours, and, although there are several points of similarity between his descriptions and the findings in the present case, there are points of difference (particularly the presence of an undoubted epithelial lining in the smaller cysts) which appear to warrant inclusion of his case in the group of true cystic lesions of the liver. Baccarini's paper contains a valuable review of the subject of cystic diseases of the liver. In contrast with Baccarini's case, that reported by Schmelling (1934) is one of multiple solid hamartomatous lesions in the liver of a male child, aged 4 months, with other congenital abnormalities.

In the discussion of a paper by Tinker (1935) on liver resection, Lund (1935) refers to the case of a woman of about 50 years, who had an " enormous " tumour, which he describes as a mass of cysts, resected from the right lobe of the liver ; no details of the pathological findings are given, but the diagnosis is said to have been congenital cystic liver.

PROGNOSIS

In view of the possibility of extensive periportal fibrosis, not necessarily detectable at operation, it is felt that the prognosis in this case must be guarded, although the reparative capacity of the liver is very great and the child, two years after operation, is in good health and without apparent disturbance of liver function or evidence of recurrence of the lesion. The latter appeared to have been completely excised, with a margin of liver.

COMMENT ON THE SURGICAL ASPECTS

Keen (1899) reviewed 76 cases of partial liver resection. At that time hæmorrhage was the most fatal complication. Warvi (1945) reviewed 223 fully reported cases of excision of primary liver tumours, and investigated some 350 others. He stated that the most serious post-operative complications were metabolic disturbances, such as early " liver failure " and late " hepato-renal syndrome ", or loss of resistance to infection, due to malnutrition, but that these could be prevented.

The presence of a pedicle-like structure in the case here reported simplified the control of hæmorrhage. The fall in plasma-proteins following operation indicated failing liver function, but normal levels were regained within three weeks, although there had been a complete biliary block for the first week. The healing of the wound following the second operation was delayed by infection.

Tumours of the liver in childhood are occasionally found to be benign, and can be resected in some cases. The early results are good, but the remote prognosis is difficult to assess. Incomplete removal of a benign tumour has been followed by recurrence and death in a matter of months. Although the prognosis is bad in the case of most liver tumours, all such cases should be explored (Ladd and Gross, 1941). In view of the fact that some tumours prove to be benign non-neoplastic lesions, this course seems all the more wise.

SUMMARY

1. The successful excision of an unusually large benign liver tumour (a cavernous lymphangiomatoid lesion, the precise nature of which remains obscure) in a child of 19 months is reported.

2. The pathology of the condition is discussed.

We wish to record our thanks to Dr. Victoria Smallpeice and to Mr. Arthur Elliot-Smith for allowing this case to be reported ; to Professor J. W. Orr and to Dr. A. H. T. Robb-Smith for the interest they have shown ; and to Dr. G. A. C. Summers for the time and care expended in producing the photographs. Our thanks are also due to the staff of the Division of Laboratories of the Radcliffe Infirmary, Oxford, and of the Department of Pathology of the University of Birmingham for laboratory investigations and technical assistance, and to Miss S. P. Katt for much help.

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VOLVULUS OF THE STOMACH

BY J. Y. W. RUSSELL

VOLVULUS of the stomach is a relatively rare condition. Buchanan (1930) reported 1 case and listed in detail 34 cases which had previously been recorded over the period 1866–1927. Gabor (1940) cited 75 cases in all. More recently several additional cases have been reported in the world's literature and the subject has been extensively reviewed and discussed by many authors.

From a survey of the literature, volvulus of the stomach resulting in perforation of the viscus would appear to be extremely uncommon. Gharpure (1939) reported 1 such case and stated that he believed it to be possibly the only one on record. It may be noted, however, that some earlier authors, including Bergmann (1897) and Buchanan (1930), have mentioned perforation as one of the possible complications of volvulus of the stomach although none of the cases listed by the latter did end in this way. It would also appear to be quite exceptional for the condition to result in a vascular occlusion

affecting the whole distribution of the superior mesenteric artery. The case to be recorded presented these two unusual features and is considered worthy of description.

CASE REPORT

HISTORY.—The patient, a married woman of 49, had been in good health until five hours prior to admission. She had been out to work in the morning and went shopping in the afternoon. She had a meal after her return home and shortly afterwards began to experience upper abdominal pain. This gradually increased in intensity and began to radiate through to the back. It remained constant and at the time of examination was still very severe. Attacks of retching followed the onset of the pain, but only small amounts of frothy vomitus without admixture of blood or bile were brought up. Bowel action had previously been regular and a normal motion had been passed earlier in the day. There had been no urinary or other abnormality.

Previous History.—The patient had had an attack of rheumatic fever when aged 12. During the last few years she had complained of slight dyspnœa on exertion and her ankles had tended to become slightly swollen in the evenings. She had had occasional attacks of vague indigestion, but had never vomited. Her weight had remained constant.

ON EXAMINATION.—On arrival at the Preston Royal Infirmary the patient was in a state of extreme shock. She was conscious but responded only very slowly and hesitantly to questions. Pallor was marked, with the mucous membranes showing a slight cyanotic tinge. Her tongue was moist and lightly coated. The pulse-rate was 150 and it was of very poor volume. The temperature was subnormal. The blood-pressure was so low that an accurate reading was not possible. The skin was cold and slightly clammy.

The abdomen was grossly and uniformly distended and was tympanitic all over, there being no evidence of any free intra-abdominal fluid. No tenderness could be elicited. The liver dullness was greatly diminished and bowel sounds were absent on auscultation. Pelvic examination revealed a sensation of fullness in the pouch of Douglas. The cervix was normally situated, but the body of the uterus could not be palpated bimanually because of the abdominal distension. Cursory examination of the central nervous system revealed normal pupillary reactions, but absent knee-jerks. No respiratory abnormality could be detected. The heart sounds were very faint, but closed and regular.

Shortly after admission to the ward a considerable quantity of dark-red blood was passed per rectum. The abdomen became more distended and reached almost barrel-like proportions. The patient began to complain of inability to move her legs and of numbness and coldness in them. Examination revealed a dusky cyanosis of the lower limbs with total loss of motor power and sensation, and absence of the deep reflexes. The shock was now even greater than on arrival and death appeared imminent.

Blood transfusion and general antishock measures were begun soon after admission, but with no real expectation that the patient would recover sufficiently to allow of operative intervention.

Death occurred four hours after admission.

AT AUTOPSY (A. A. M.).—

External Examination.—The body was that of a well-nourished, healthy, female adult with a greatly distended abdomen.

Internal Examination.—

Thorax: The left lung was bound to the chest wall by firm, fibrous adhesions. Both lungs were normal in size and showed slight congestion only.

The heart showed no macroscopic abnormality.

Abdomen: On opening the peritoneal cavity there was free escape of gas. Streaks of blood-clot were seen at the left costal margin. An enormous rounded tumour which filled the whole upper abdomen was found to be the stomach twisted on its vascular pedicle, the pyloric antrum lying beneath the left dome of the diaphragm. On releasing the volvulus gas escaped freely from the distended stomach into the duodenum. The cardiac end was congested and almost black in colour. About eight to ten ounces of unclotted blood and also some blood-clot were found beneath the left diaphragm and around the spleen.

The *stomach* contained about one pint of dark green watery fluid with admixture of undigested lumps of potato and meat. Some of the lumps were up to 2 to 3 cm. in their longest diameter. The stomach wall was thin, stretched, partly ulcerated, and necrotic. There was a very large ill-defined non-viable area on the lesser curvature in which there was a large central ulcerated patch measuring 5 × 7 cm. More superficial ulceration extended for 5 cm. from the patch towards the pyloric end. There were numerous breaks in the mucosa, triangular, oval, and of irregular shape. The adjacent

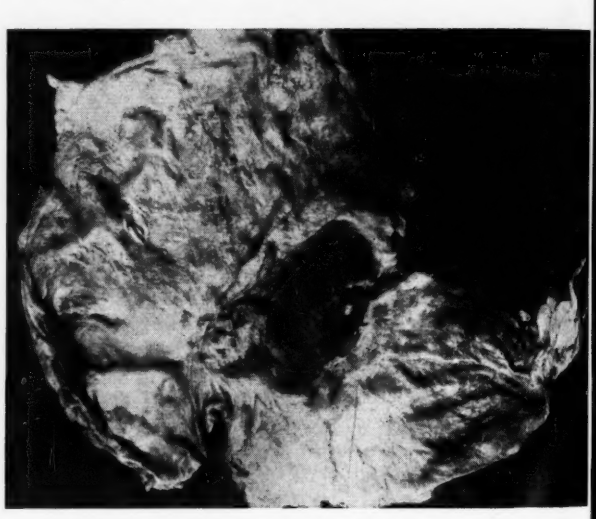

FIG. 22.—Interior of stomach showing large ulcerated area on lesser curvature. The cardiac end is above and to the right.

mucosa was reddish purple and black in appearance. There was incipient gangrene, especially at the cardiac end (*Fig.* 22).

Intestines: There was marked congestion of the duodenum, jejunum, ileum, and proximal colon, i.e., throughout the distribution of the superior mesenteric artery. There were hæmorrhages into the gut wall and a considerable amount of free blood in the lumen.

The spleen was enlarged and the capsule smooth. Cross-section showed marked passive congestion.

The liver was of normal size and pattern but was congested.

The right kidney was smaller than normal; the left was normal in size and had a double ureter. Both kidneys showed acute passive congestion.

The adrenals showed no abnormality.

HISTOLOGY.—

Stomach: The sections show stretching and thinning of all structures. The mucosa shows superficial degenerative changes throughout and in one area is completely necrotic. Much of the muscle shows early degenerative changes, but there is no evidence of active inflammation.

Spleen: This shows a typical septic reaction with congestion and hyperplasia of the follicles.

DISCUSSION

As volvulus of the stomach has been extensively reviewed by many authors, in this paper it is not intended to discuss the subject in detail.

The clinical features of this case were not observed until a late stage had been reached, and the abdominal condition tended to be obscured by the extreme state of collapse which had supervened. Pain is generally the earliest symptom of gastric volvulus and may be excruciating. It is usually situated in the epigastrium but may be referred to the back, presumably as a result of pull on the mesenteries. As in this case, vomiting or retching are often associated and the vomitus is never found to contain any bile. Any ingested material is, as a rule, promptly returned unaltered. At an early stage a smooth, uniform, rounded and tympanitic gastric swelling can be made out in the upper abdomen. When this case was seen this swelling could not be detected as it was completely masked by the generalized abdominal distension which was present. This was caused by escape of gas through the ulcerated stomach wall, resulting in a marked tympanitic percussion note and the total disappearance of liver dullness and bowel sounds. It may be noted that no macroscopic defect in the stomach wall could be made out, but it can be presumed with certainty that leakage did occur through a minute defect in the overdistended stomach which became invisible after the escape and consequent shrinking of the stomach.

When the stomach is intact there is usually little evidence of peritoneal irritation with tenderness, hyperæsthesia, and muscular guarding.

The melæna was due to the associated superior mesenteric vascular occlusion. In this, the passage of blood occurs in some 50 per cent of cases, according to Cokkinis (1926). Mayo, Miller, and Stalker (1940) state that occult blood is uniformly present in the stools in the venous type of thrombosis. Elliott, quoted by Harkins (1936), found it present in 13 out of 20 cases. Where the small gut alone is involved, some blood in the infarcted segment is usually propelled into the large gut before ileus sets in, and can be washed out by a high enema. In this case the right half of the colon, as well as the whole of the small intestine, was involved and a great deal of blood was present in the lumen of the gut.

A considerable degree of shock in gastric volvulus is common and is due to the overstretching of the gut wall along with the pull on the mesenteries and pressure on adjacent viscera, but the extreme collapse which was present in this case is seldom encountered. It is considered that the excessive shock was attributable, partly to the presence of the gastric perforation with the escape of gastric contents into the peritoneum, partly to the hæmorrhage around the splenic pedicle, but in greatest part to the total superior mesenteric occlusion. The severe degree of shock which can be produced by even small leaks from a peptic ulcer or small mesenteric occlusions is well known.

In milder cases of volvulus the symptoms may be intermittent and may be relieved by alteration of the patient's position. Cardon, Greenbaum, and Arendt (1947) record a case in which relief was obtained by lying prone across a bed with the trunk hanging over the edge at right angles to the lower extremities.

Diagnosis.—This presented considerable difficulty. The melæna suggested a mesenteric vascular occlusion and the massive distension a volvulus. The coldness, lack of pulsation, and apparent paralysis in the lower limbs were difficult to explain. Some massive vascular accident of the nature of rupture of an intra-abdominal aneurysm was mooted and considered a possibility, although it could not account for the gaseous distension.

The insertion of a hollow needle through the abdominal wall, as recommended by some surgeons for diagnostic purposes in cases of perforated hollow viscus, would undoubtedly have been of some value in clarifying the picture, as the still grossly distended stomach would probably have become palpable with escape of the intraperitoneal gas.

A ' straight ' X-ray film of the abdomen should be carried out in all suspected cases as the large gastric air shadow can as a rule be identified.

Pathology.—Various classifications of the types of gastric volvulus have been suggested. According to Buchanan's classification, this was a case of volvulus mesenterio-axialis in which the stomach has twisted on an axis at right angles to a line joining the cardia and pylorus. The main movement in this type is by the pyloric end of the stomach, which is unduly mobile. Buchanan (1930) maintains that this always passes anterior to the fundal end from the right, upwards and to the left, but Singleton (1940) states that it may pass posteriorly. The anterior wall of the stomach is sharply kinked on itself and now looks backward and to the left, while the posterior wall presents under the abdominal wall, veiled in the majority of cases by omentum. The pylorus now lies under the left dome of the diaphragm, while the cardia and adjacent œsophagus lie under the right costal margin. The displacement of other organs in this type is usually not very marked. The duodenum, together with the head of the pancreas and the transverse colon, is drawn upwards and medially towards the left costal margin. In some cases the colon may be acutely kinked.

Distension takes place when the pylorus and cardia become occluded. It is due to the retention of stomach contents, to hypersecretion, and, when the venous pressure rises, to transudation.

The other main type is volvulus organo-axialis in which the axis of rotation is in the line joining the pyloric and cardiac orifices. Rotation may be anterior or posterior. In the more common form the greater curvature rotates upwards in front of the lesser, so that the posterior surface of the stomach comes to lie anteriorly.

Either of these two types may be partial or total. In partial volvulus there is very much less distension and as a rule no marked interference with the gastric blood-supply at any stage. In this case the volvulus was total.

It would seem that the rotation was to some extent centred on the cœliac axis and when it occurred there is little doubt that the vascular supply to the stomach was interfered with by the twisting of the vascular pedicle. It is considered that the extensive ulceration was probably due to a combination of three

factors—ischæmic necrosis, overstretching by distension, and shearing torsional strain. Ulceration is not very common in gastric volvulus and it would appear that the extent of the ulceration in this case was quite exceptional. Some authors write of gastric "erosions". Science (1938) describes a case in which there were two ulcers lying saddle-shaped across the lesser curvature in the juxta-pyloric region, one of ½-in. and one of ¾-in. diameter.

The origin of the superior mesenteric artery is only about 1 cm. from the cœliac axis. It is quite understandable that when this is twisted the mesenteric vessel may be involved and occluded. An alternative explanation for the mesenteric infarction is that the mesenteric vessels were nipped at the point where they lie in front of the third part of the duodenum, when this and the colon were pulled forcibly upwards and to the left by the rotating pylorus.

Hæmorrhage is encountered in some cases of gastric volvulus and may be severe. Borchardt (quoted by Buchanan) had to carry out splenectomy in his case for rupture of the splenic vessels. In this case a considerable amount of fresh blood was present under the left dome of the diaphragm and may have come from the splenic vessels.

Other complications which have been encountered include necrosis of the pancreas from rupture, and avulsion of the omenta, the greater omentum in one reported case having been completely torn from the greater curvature.

Aetiology.—In this case the predisposing factors would appear to be the existence of abnormally long gastric ligaments with excessive gastric mobility, and the presence of a recently ingested, poorly masticated, heavy meal with the presumed production of vigorous peristalsis.

These are commonly cited as the main factors in the production of the idiopathic variety of volvulus which is usually total and acute.

Other factors which are sometimes concerned may be 'extrinsic', such as diaphragmatic herniæ, elevation of the diaphragm after pneumonectomy, or congenital defects in the mesocolon or omenta; or 'intrinsic' such as peptic ulcers, tumours, or scars. The volvulus in these cases is usually partial. French writers have in some cases attributed the condition to overdistension of the colon ('*ærocolie*'). Cardon and others (1947) have described a case in which sudden increase of intra-abdominal tension due to heavy lifting appeared to be the precipitating factor.

Treatment.—In the first place an effort should be made to pass a stomach tube. If this can be made to enter the stomach, aspiration of the gastric contents relieves the condition, spontaneous untwisting taking place. As Bickham (1924) states, however, the passage of a tube is generally impossible, the impossibility being a diagnostic measure. If the stomach cannot be entered, if signs of obstruction and strangulation persist, or if other complications supervene, then operation should be performed. Anagnostides (1935) recorded 28 recoveries in 48 cases operated on. Hill and Paul (1939) reported that there had been 60 per cent of recoveries in such cases. They recommend emptying the stomach with a trocar and cannula after exposure, but stress the importance of immediate closure of the site of the puncture prior to untwisting the stomach as it may pass to an inaccessible position. After emptying the reduction may be very easy. It may be noted that Bergmann (1897) stated that he thought it possible that cases of idiopathic rupture of the stomach may in reality have been cases of volvulus in which spontaneous rupture led to reduction. Subsequent treatment will depend on the cause of the volvulus, e.g., gastrectomy for neoplasm, or on the presence of complications. In idiopathic uncomplicated cases some effort should be made to fix the stomach to prevent recurrence of the condition. Gastropexy procedures, such as Beyea's operation of lesser omental plication and Coffey's suspension of the stomach by an omental hammock, have been described.

SUMMARY

1. A case of volvulus of the stomach is reported.

2. It is thought that this may be the second recorded case of perforation in association with gastric volvulus.

3. It may possibly be unique in respect of the superior mesenteric vascular occlusion which was present.

4. The diagnosis, pathology, aetiology, and treatment of the condition are briefly discussed.

I should like to express my thanks to Mr. Ian M. Orr for permission to publish this case; and to Dr. A. A. Miller, who performed the post-mortem examination. I acknowledge in addition their helpful criticism of this paper.

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OBSERVATIONS ON BILE-ACID ENTEROLITHS
WITH AN ACCOUNT OF A RECENT CASE

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Bile-salts, like cholesterol and bile-pigments, are normal constituents of bile, but while solid deposits containing cholesterol and bile-pigments, i.e., gall-stones, are common, solid deposits of bile-salts do not occur. This is because the bile-salts are very soluble in water and body fluids. The free bile-acids, however, are relatively insoluble, and are readily deposited from solutions containing bile-salts if these solutions are made sufficiently acid.

Other factors, as well as a sufficient degree of acidity, are required if precipitated bile-acids are to be retained as a cohesive aggregate or stone. All the necessary factors are evidently present occasionally, for a few cases of bile-acid enteroliths are on record.

The principal bile-acids whose salts are normally present in human bile are cholic acid and deoxycholic acid; one, which is less well known, chenodeoxycholic acid, may also be present, sometimes in appreciable amounts. It is believed that the greater part of these acids is conjugated with the amino-acids glycine and taurine, forming glyco- or tauro-cholic acid, glyco- or tauro-deoxycholic acid, etc., and it is the salts of the glyco- or tauro-acids which are usually referred to as the bile-salts. Deoxycholic acid differs from the other two in possessing to a very high degree, in its free or unconjugated form, the property of forming molecular compounds with a number of other substances. Of special importance are the compounds it forms with the higher fatty acids, particularly palmitic and stearic acids. These compounds, known as choleic acids, contain eight molecules of deoxycholic acid and one of the fatty acid. Probably most, if not all, of the unconjugated deoxycholic acid which finds its way into the intestine is in the form of choleic acid.

Enteroliths consisting mainly of choleic acid have been reported on at least ten occasions, the first by K. A. H. Mörner and Sjöquist in 1908 (quoted by C. T. Mörner, 1923). C. T. Mörner (1939) gives a list of cases known to him up to that time. The only case reported from this country is the one described by Raper (1921) and by Phillips (1921), the remainder having been found in Sweden. Chitre and Puradare (1944) described an enterolith weighing 185·5 g., removed from a Hindu woman, which was said to contain over 70 per cent of glycocholic acid, but no details of the analysis nor physical constants of the bile-acid were given.

Recently two large enteroliths consisting very largely of choleic acid were removed from the intestine of a woman patient under the care of one of us (G. A.). It is our present intention to describe this case, and then to discuss the factors which seem to us to be of importance in determining the formation of these interesting stones, for, as we hope to show later, they are very probably of more frequent occurrence than is indicated by the small number of reported cases.

CASE REPORT

Mrs. E. H., aged 73 years, referred by Dr. Ralph Hodgson, was admitted to hospital on March 6, 1948, as an emergency complaining of severe colicky abdominal pain. Six similar attacks had occurred paroxysmally during the past year. At first, each attack would come on suddenly and last for about one hour. More recently the attacks had increased in severity and duration and had been associated with vomiting, as frequently as fifteen times per day. The present attack was the most severe, and had lasted for three days. Between the attacks of abdominal pain there had been considerable flatulence and heartburn.

On Examination.—The patient looked ill, the pulse-rate was slightly raised, there was no pyrexia, and respirations were normal. There was slight abdominal distension but no tenderness in the hypochondrium. She complained of some pain across the small of the back. It is interesting to record that the patient's husband, who had suffered from gall-stone colic with jaundice and who had been operated upon by one of us (G. A.) thirteen years previously, was emphatic in his belief that his wife's pain was not of the same nature as that from which he had suffered. We were impressed by this observation, which proved later to be so significant.

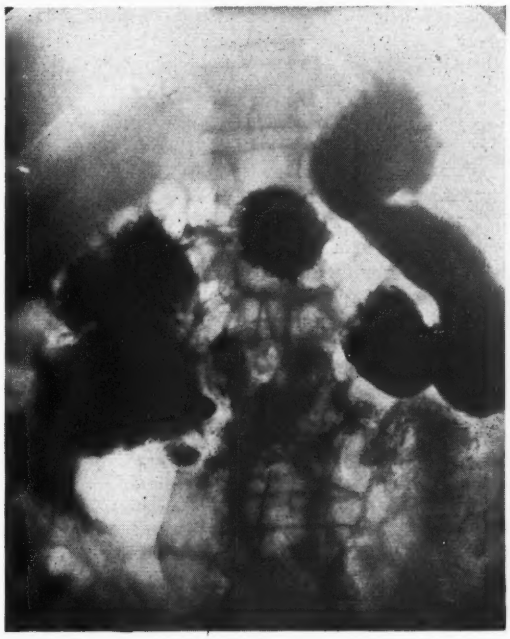

Fig. 23.—Barium outlines the stomach. The duodenal cap overlies the spine. Several large diverticula arising from the second and third parts are filled with barium. The barium has entered the upper jejunum, which at this stage appeared normal. Gas-distended coils of small bowel are seen below the duodenum.

A tentative diagnosis of subacute pancreatitis, intestinal obstruction, or gall-stones was made, and in view of the good general condition it was decided to watch her carefully.

With dramatic suddenness pain and vomiting disappeared at the end of 72 hours, flatus was passed, and general improvement took place. There was no leucocytosis.

Radiological investigation was carried out by one of us (A. S. J.).

It was decided to prepare the patient for cholecystography and screen her at the time of taking the straight film. If any evidence of pyloric obstruction was obtained

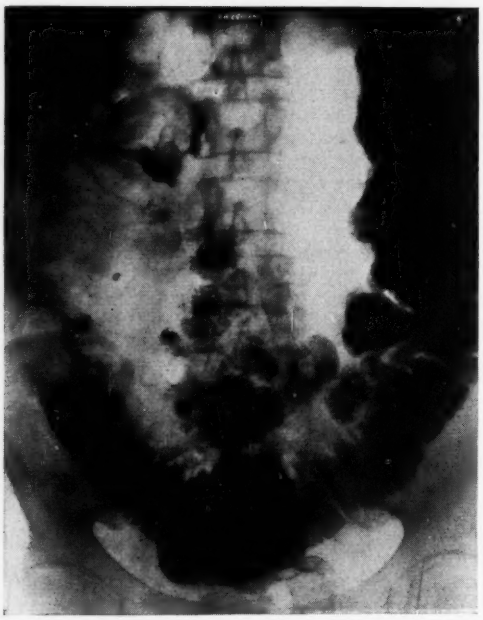

FIG. 24.—The barium is held up in a coil of ileum by a kidney-shaped defect seen over the right iliac crest. This was thought to be a tumour. Note a ring opacity to the right of the second lumbar vertebra. This was caused by the large enterolith lying in a diverticulum which had previously been obscured by barium. As emptying occurred traces remained to outline the stone. The significance of these findings was not apparent until after reviewing the films in the light of operative findings.

then the cholecystography would be postponed and a barium meal given.

On screening there was no evidence of obstruction. The stomach appeared to be empty. There were, however, several coils of gas-filled small bowel in the right lumbar quadrant, but no fluid levels and no peristalsis.

The cholecystography was completed and the gall-bladder appeared to function normally. There was no evidence of calculi. Gas was still evident in the small bowel and the coils appeared to be thickened as if matted by some plastic peritonitis.

The barium meal was given one day later.

Screening of the chest showed no definite abnormality. The œsophagus appeared to be normal. The stomach was normal in size, shape, and outline, but was displaced to the left. The first part of the duodenum was elongated and stretched across the spine in a manner which suggested a pancreatic tumour, but the sudden filling of several large duodenal diverticula immediately corrected this impression (*Fig.* 23). These diverticula appeared to arise from the second and third parts. The lateral view showed that some passed behind the head of the pancreas while others emerged anterior to it. Although delay in emptying these sacs was anticipated, all except one were clear of barium at six hours. The passage through the small bowel was slow. Several diverticula were seen in the upper jejunum. At 24 hours residues of barium were traced through the colon but the bulk of the meal was still in the small bowel, demonstrating clearly a loop of ileum slightly dilated, which ended abruptly in the right flank. At the termination there was a filling defect resembling a rounded mass which was thought to be a tumour. Residues were still present in one duodenal diverticulum, outlining a large filling defect. The significance was not appreciated until after the laparotomy. (*Fig.* 24.)

Another confusing feature was provided by the rounded masses of barium which lay around the mid-abdomen. These were thought to be residues in sacculations of the colon, whereas they were residues in enormous jejunal diverticula (*Fig.* 25).

FIG. 25.—Showing large jejunal diverticula. The enterolith in the duodenal diverticulum is apparent (marked with arrow).

It should be noted that the calculi found at operation were not radio-opaque.

A diagnosis of chronic ileal obstruction was made, thought to be due, perhaps, to a plastic peritonitis resulting from a leaking diverticulum.

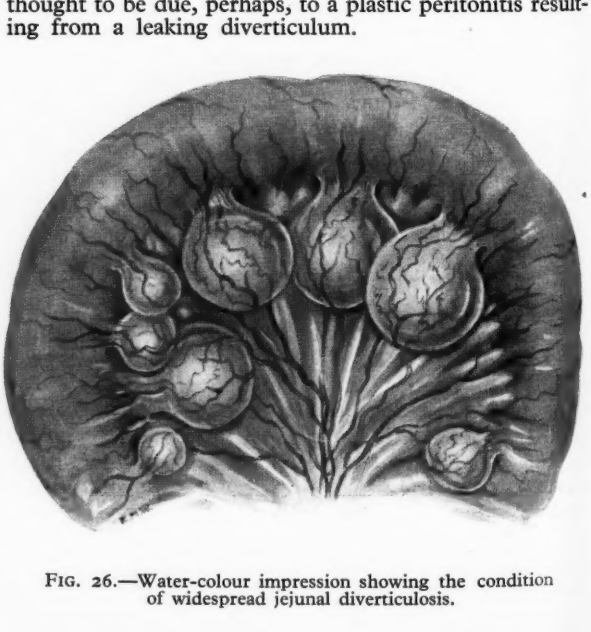

FIG. 26.—Water-colour impression showing the condition of widespread jejunal diverticulosis.

AT OPERATION.—Laparotomy was decided upon and carried out on March 21.

On opening the peritoneal cavity distended coils of jejunum and ileum presented a picture of widespread diverticulosis (*Fig.* 26). The distension of the ileum ceased abruptly at a point 2 ft. above the ileocæcal junction, where a large hard enterolith was felt. The ileum was opened and a stone, shaped somewhat like a spleen and covered with greenish bile, was removed. This was thought to be a gall-stone, though admittedly of unusual shape. It weighed 26 g. and measured 41 × 21 × 35 mm. (*Fig.* 27). The gall-bladder was

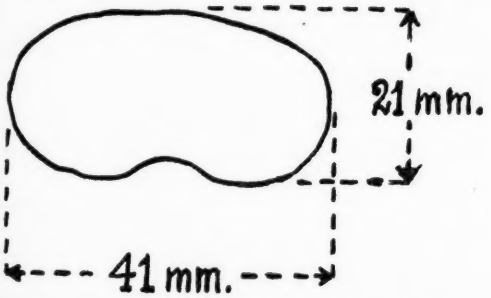

FIG. 27.—Section of smaller stone removed from the ileum.

next examined and found to be normal, confirming the cholecystography. Whilst doing this another stone was felt in the region of the second part of the duodenum, and this was found to be contained in the large duodenal diverticulum previously noted. In order to remove this stone the diverticulum and duodenum were opened. The stone was shaped rather like the astragalus, the larger end being in the diverticulum and the smaller end in the second part of the duodenum. It weighed 29 g. and measured 47 × 45 × 30 mm. (*Fig.* 28).

Penicillin-sulphonamide powder was insufflated into the peritoneal cavity and the abdomen was closed without drainage.

Post-operative recovery was uneventful, and the patient is now quite well.

Comment.—On considering the case after operation, it seems quite evident that the enterolith found in the ileum had been alternately impacting and releasing itself, thereby causing the attacks of severe pain; it would appear that this enterolith, too, was of diverticular origin.

Chemical analysis of the stones showed that they contained over 90 per cent of bile-acid, the remainder being fat, fatty acid, and food residues. Of the bile-acid, approximately 90 per cent was choleic acid, and 10 per cent was cholic acid. The mineral matter amounted to only about 0·4 per cent, which explains why the stones were not opaque to X rays. At the centre of the larger stone was a piece of vegetable matter, probably fruit skin. Full details of the chemical analysis have been published elsewhere (Fowweather, 1949).

DISCUSSION

True enteroliths of any kind are rare. When one considers the ease with which many foreign bodies pass through the normal alimentary canal, it is obvious that for enteroliths to form and grow in size some mechanical condition must be present which allows of the retention of concretions within the intestine in their early stages. In practically all the reported cases such mechanical condition was noted; in some the stones were obviously related to the presence of diverticula, in a few to stricture. Diverticula of the small intestine are generally considered to be rare, but there is some evidence to suggest that they are commoner than is usually supposed. Thus Wheeler (quoted by Shaw, 1940), in a consecutive series of 2000 barium examinations, found 7·1 per cent of primary duodenal diverticula. Edwards (1935), however, gave figures very much lower than this. The presence of foreign bodies is also likely to be favourable to stone formation since their presence will cause stasis—an important factor

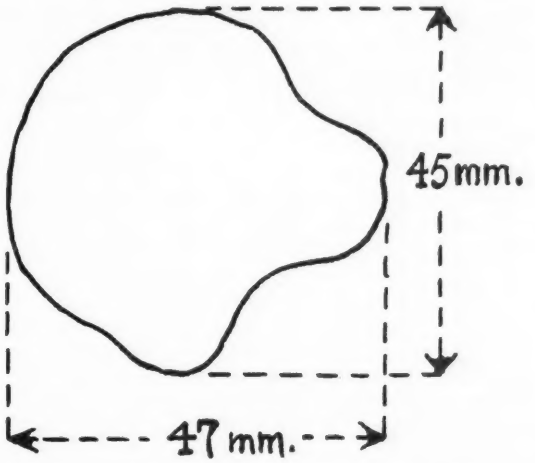

FIG. 28.—Section of larger stone removed from the duodenal diverticulum.

in stone formation—either in a diverticulum or in the lumen of the intestine, and they will also act as a nucleus around which solid material may be deposited. Helström (1936) found a plum-stone at the centre of a choleic acid enterolith. Raper found tissue resembling fruit skin; similar material was found in the larger of the two stones in the present case, and Chitre and Puradare found a tamarind seed.

There must be in addition special conditions which determine the formation of bile-acid stones. The reported cases already referred to have, with one exception, been choleic-acid stones, and the exception, that of Chitre and Puradare, is not sufficiently well documented to place the identification of the bile-acid concerned entirely beyond doubt. This finding at first seems surprising, since the conjugated bile-acids are normally present in much greater concentration than choleic acid. An experiment was carried out by one of us (F. S. F.) to determine the *p*H at which choleic acid, cholic acid, and glycocholic acid were precipitated from solutions of their sodium salts, and the following results were obtained :—

Bile-acid	*pH at which Precipitation had Occurred*
Choleic acid	7·0
Cholic acid	5·8–6·0
Glycocholic acid	4·6–4·8

McGee and Hastings (1942), in experiments on human subjects, found that the *p*H of the upper part of the small intestine was between 6·2 and 6·8, except in a few isolated instances. The results of the above experiment show that choleic acid is the only one of those examined which will be precipitated within this range, and thus offer a convincing explanation why choleic acid is precipitated in

preference to other bile-acids. It is probable that in some cases the acidity in this region exceeds the normal (e.g., when the amount of HCl discharged from the stomach into the duodenum is greater than usual, as in conditions associated with hyperchlorhydria) and may reach a degree of acidity sufficient to cause precipitation of cholic acid also, but the attainment of an acidity sufficient to precipitate glyco- or tauro-acids is very much less likely.

But the formation of stones within the intestine would appear to require the precipitation of the material concerned in appreciable quantity, yet it is believed that unconjugated bile-acids are present in bile in quite small amounts. Doubilet (1936) gives some results of " typical examples " of differential bile-acid analysis; these show, in human gall-bladder bile, 0·890 per cent of unconjugated acids, out of a total of 9·751 per cent, and in human fistula bile 0·413 per cent out of a total of 1·717 per cent. Not all of the unconjugated acids is deoxycholic acid, capable of combination with the free fatty acid in bile or in the intestine to form choleic acid. We have not seen any separate figures for unconjugated cholic and deoxycholic acid in bile, but it is generally believed that the total cholic acid exceeds the total deoxycholic acid. Wieland and Reverey (1924), who noted the presence of chenodeoxycholic acid in human bile, gave the proportions of cholic : deoxycholic : cheno-deoxycholic acid as 3 : 1 : 1. Doubilet's figures for human gall-bladder bile show 4·255 per cent of cholic acid and 5·496 per cent of deoxycholic acid; he makes no mention of chenodeoxycholic acid, but if any were present it would be included in the figure for deoxycholic acid. Here it may be noted that Nagaki and Ohyama (quoted by Saba, 1940) claim that cheno-deoxycholic acid is often found to predominate in human bile. Figures for deoxycholic acid, therefore, in cases in which examination for, or determination of, cheno-deoxycholic acid is not made, may well be too high. Cheno-deoxycholic acid, like cholic acid, has little tendency to form molecular compounds such as are formed by deoxycholic acid (Sobotka, 1937, a); hence its presence will not result in the formation of choleic acid. If, then, the proportion of unconjugated deoxycholic acid in bile bears any relation to that of the total deoxycholic acid, the amount of the former—and therefore of choleic acid—is normally very small; it is in fact so small as to suggest that deposition and retention within the intestine, in quantities sufficient to form the enteroliths which have been described, are unlikely to occur.

There are, however, certain considerations which suggest that in some cases the choleic acid of the bile may be higher than is suggested by the figures already quoted. In the first place, the number of published differential bile-acid analyses of human bile is small, and gives no indication of the variations which might occur normally in the amount and proportion of different acids; in this connexion it has also to be remembered that the methods of analysis available for this purpose leave much to be desired. In the second place, there is some evidence that the proportion of conjugated to unconjugated bile-acid, and of cholic acid to deoxycholic acid, etc., may be altered by disease. The liver is presumably the site of conjugation, and an increase in unconjugated bile-acid has been noted in disease of that organ (Sobotka, 1937, b). An increase in the proportion of deoxycholic acid to cholic acid has also been noted, mainly in pathological conditions, but Sobotka thinks this is more likely to be due to a decrease in production of cholic acid than to an increase of deoxycholic acid. Disease of the gall-bladder, by altering its capacity to absorb various substances from bile, may also alter the bile-acid composition of this fluid.

It will be seen, therefore, that the formation of choleic-acid stones requires the concurrence of a number of factors—viz., a mechanical condition capable of allowing the retention of precipitated acid, bile which contains more deoxycholic acid than is usually present, and, too, bile which contains a considerable proportion of deoxycholic acid in the unconjugated form. Whether these bile changes represent the extreme of normal variation or are the result of disease cannot be decided on our present knowledge of the bile-acid composition of bile. Hyperchlorhydria may be an additional factor. Retention within the intestine of indigestible material is also of some importance.

One other fact has not yet been considered, namely, that all the reported cases have occurred in women. Why this should be so is not clear, and can only be a matter for speculation. One is reminded that the incidence of gall-stones is much greater in women than in men. Foss and Summers (1942) say that the relative incidence is generally given as five or six to one. Earlier writers give a lower ratio; thus the figures of Chauffard (1922) place it at less than three to one. Most writers consider that cholecystitis is an important factor in the production of gall-stones, and this, too, is commoner in women. Chauffard believes that the greater incidence of gall-stones in women can only be explained by physiological differences between the sexes.

It does seem possible that some connexion may exist between the greater liability of women to produce gall-stones and bile-acid enteroliths, but whether this may be due to related physiological disturbances, to their greater liability to suffer from biliary disease, or to quite different factors is not known.

The fact that the production of choleic-acid enteroliths requires the concurrence of a number of factors explains their rarity. Nevertheless, certain considerations suggest that they may not be so rare as might be supposed. Of the 10 previously reported cases, 5 have been recorded by one man (C. T. Mörner, 1939) and 3 by another (Helström, 1936). That one keen observer should have identified half the known cases does seem to show that others must have been missed, and there is much evidence that some enteroliths have not been examined at all, or have received insufficient examination to identify their constituents with certainty.

Phillips (1921) reported enteroliths in two patients who came under his care within a period of five months. The second patient was a woman of 68, and the stone, which was found in a coil of small gut—apparently about the middle of the jejunum—was clearly a choleic-acid enterolith; it is the one which was examined and reported on by Raper (1921). The first patient was a woman of 65; the stone was

found near the lower end of the ileum and had a plum-stone at its centre. It was examined by a public analyst, who found that it contained 2·6 per cent of moisture and less than 0·1 per cent of ash. The dry organic matter contained :—

	per cent
Carbon	71·17
Hydrogen	10·87
Oxygen	17·26
Nitrogen	0·29
Sulphur	0·39

The analyst's interpretation of these figures is entirely unconvincing, but it is of interest to note that, for choleic acid, theoretical figures are :—

	per cent
Carbon	73·6
Hydrogen	10·4
Oxygen	16·0

The correspondence between these sets of figures is sufficiently close to suggest the possibility that the material analysed may have been impure choleic acid.

Kelly (1932) removed from a woman three enteroliths found in a dilated coil of jejunum which had a stricture at each end. The pathologist's report on these stones says that " the evidence is in favour of organic material, largely fats and soaps which have been formed in situ ". The evidence referred to, however, hardly bears out this conclusion, as the material examined was readily soluble in alcohol, and inorganic matter was scanty. Neutral fat is soluble with difficulty in alcohol and the soaps found in the intestine are largely calcium soaps, which are insoluble in alcohol ; moreover, if soaps were present to any considerable extent, inorganic matter (ash) would not be scanty. The stone did not contain cholesterol. Shaw (1940) removed from a woman a stone which was believed to have been formed in and which extruded from a large duodenal diverticulum. The only information as to the nature of the stone is that " its chemical analysis was mainly lipoid material with traces of cholesterol, uric acid, phospho-lipins, calcium soaps, and bile-pigments ". Watson (1924) removed a portion of jejunum containing a diverticulum in which was a " large " enterolith, from a man aged 73, but makes no mention of the nature of the stone. Allen and Donaldson (1945), recording a case of calculi in Meckel's diverticulum, simply describe the stones as " large, hard, bile-stained concretions ". With reference to 11 such cases collected by them they refer to " the one case in which chemical analysis was reported ".

Intestinal obstruction due to gall-stones is a well-recognized condition, forming, according to various reports, from 1 to 5 per cent of all cases of intestinal obstruction, with a female to male ratio of 6·5 to 1. Foss and Summers (1942), in discussing the differential diagnosis of this condition, do not include enteroliths, no doubt because, if obstruction is produced by a stone, its chemical nature is of no immediate clinical importance. It is very probable that, when a stone is found to be the cause of intestinal obstruction, most surgeons assume that the stone is a gall-stone, and no analysis of it is made. The assumption is no doubt correct in most cases, but it may be that on occasion a true enterolith, perhaps consisting mainly of bile-acid, is overlooked. Any real knowledge of the incidence of bile-acid enteroliths—or indeed of any type of enterolith—can only be obtained if all stones found in the intestine are submitted to most careful chemical analysis.

SUMMARY

1. The case of a woman who showed widespread duodenal and jejunal diverticulosis, and from whom two large choleic-acid enteroliths were removed, has been described.

2. The factors which may be responsible for the formation of choleic-acid enteroliths have been discussed. It has been shown that, of the bile-acids usually present, choleic acid is much the most likely one to be precipitated at the reaction normally found at the site of formation of these enteroliths.

3. Such enteroliths are unlikely to be produced unless the choleic-acid content of the bile is greater than that usually found. Whether this change in the bile composition is due to hepatic or biliary disease, or is within the limits of normal variation, cannot be decided on our present knowledge.

Other probable factors are hyperchlorhydria and the presence of retained indigestible material in the upper part of the small intestine.

4. While bile-acid enteroliths are undoubtedly of rare occurrence, it is shown that they are probably commoner than the number of reported cases indicates. This is believed to be due to insufficient examination of intestinal stones in some cases, and lack of any examination in others. Careful chemical examination of all intestinal stones is recommended.

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SARCOMA BOTRYOIDES OF THE GENITAL TRACT IN FEMALE CHILDREN

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Sarcoma botryoides, a descriptive term, is said by Tracy (1930) to have first been used by Gersant in 1854. It describes a malignant mesodermal tumour, like a bunch of grapes, which arises from the lower part of the female genital tract both in adults and in children. McFarland (1935) summarizes the age incidence of this tumour as in *Table I.*

Table. I.—Incidence of Sarcoma Botryoides. (*After McFarland*, 1935)

Site	Under 2 Years of Age	Up to 22 Years of Age	Over 22 Years of Age
Vaginal	42	74	0
Uterine	5	22	39

Early references to the disease are to be found chiefly in the Austrian and German literature (Anderson and Edmannson, 1869; Mönckeberg, 1874; Conheim, 1875; Pfannenstiehl, 1892; Nehrkorn, 1898; Wilms, 1899); indeed, Glynn and Blair-Bell (1914) stated that no case had been reported in the British literature prior to their presentation—though they seem to have overlooked an earlier English report by D'Arcy Power (1895). They also omitted reference to the detailed study of sarcoma of the vagina by McFarland (1911) in the United States.

In the ensuing years, Wilfred Shaw (1928), Adler (1928), Brumwell (1929), Tracy (1930), Dugge (1930), Shapiro (1931), Owen (1933), Lochrane (1933), McFarland (1935), Harding and Hankins (1937), Novak and Anderson (1937), Amolsch (1939), Duggan (1939), Campbell (1940), Gunning and Ross (1940), Poole (1943), Dwyer (1944), Ulfelder and Quan (1947), and Fasanotti (1948) added to the literature on the subject, but in the main they presented one or more case reports of the disease occurring either in children or adults, and recapitulated previous studies of the origin of the tumour and its pathology. The papers by Wilfred Shaw (1928), Adler (1928), and McFarland (1935) are outstanding, and, supplemented by the section on the subject in Willis's *Pathology of Tumours* (1948), they constitute an authoritative summation of what is now known of the disease.

Pathology.—Wilfred Shaw (1928) has classified the malignant mesodermal tumours of the female genital tract according to their site of origin in the body of the uterus, the cervix, and the vagina. He refers to them as mixed tumours of the uterus and vagina and distinguishes (1) those which arise in the body of the uterus, occur usually after the menopause, and are polypoidal, papillary, or lobulated in character, from (2) those which arise from the cervix, are of more frequent occurrence, occur in patients from the age of 17 to 52 years, and appear typically as grape-like tumours, and from (3) the polypoidal sarcoma botryoides of the vagina which occurs in very young children.

Sarcoma botryoides of the vagina is recorded as being present in a child at birth (Martin, Williams, and Bowers, quoted by McFarland, 1935), while

Table II.—Outcomf of Recorded Cases of Sarcoma Botryoides in Children up to 1949

Author	Date	No. of Cases	Age	Course of Disease
Glynn and Blair-Bell	1914	2	(1) 2½ yr.	Died 6 mth. Cachexia
			(2) 2¼ yr.	Died 2 yr. Local recurrence.
Adler	1928	37	—	Majority died shortly. Three lived 2 or more yr.
Shaw	1928	1	3½ yr.	Died rapidly. X-ray therapy
Brumwell	1929	1	1 yr. 1 mth.	Recurrence at 1 yr. 10 mth.
				Well " " 2 yr. 2 mth.
				" " 2 yr. 9 mth. (local excision and radium)
Owen	1933	1	4 yr.	Died 3 mth. Pelvic peritonitis. Right hydronephrosis. Necrosis of liver. Retention of urine
McFarland	1935	1	6 yr.	Died 10 mth. Local recurrence. Local pelvic spread
Novak and Anderson	1937	2	(1) 7 mth.	Died
			(2) 2 yr.	Died shortly
Harding and Hankins	1937	1	3 yr.	Died 5 wk. Local recurrence. Involvement of ureters. Anuria
Amolsch	1939	1	2½ yr.	Died 1 yr. 1 mth. after onset of symptoms. Retroperitoneal iliac metastases
Dwyer	1944	1	1 yr. 9 mth.	Died 7 mth. Perforated bladder. Pelvic abscess. Bilateral hydronephrosis
Ulfelder and Quan	1947	1	2½ yr.	Catheterization for residual urine for 3 mth.
Willis	1948	2	(1) 2 yr.	Died 4 mth. Pelvic spread. Metastases in lymph-nodes, peritoneum, and lungs
			(2) 6 yr.	Died 2½ mth. Growth replaced base of the bladder and urethra
Fasanotti	1948	2	(1) 6 yr.	Died 3 mth. Recurrence after local removal
			(2) 3 yr.	Died 6 mth.
Author's case	1949	1	4 yr.	

similar grape-like tumours have been described in other patients arising from the skeletal musculature, the palate, œsophagus, suprarenal, ovary, bladder, prostate, spermatic cord, lungs, and the breasts.

The vaginal tumour may originate in the anterior wall, the posterior wall, or the region of the hymen (Amolsch, 1939). The commonest site of origin is said to be the region of the anterior fornix (Willis, 1948). In its naked-eye appearance the vaginal tumour consists of grape-like, œdematous, moist, polypoid fleshy masses hanging down into the vagina and sometimes protruding between the labia. Superficial necrosis may be present with bleeding and vaginal discharge. The growth may distend the vagina or infiltrate the rectovaginal or vesicovaginal septum. It may penetrate and perforate the uterine wall and cause fatal peritonitis (Glynn and Blair-Bell, 1914). Spread may occur into the parametrium and the pelvis. Ureteric dilatation has followed obstruction of the bladder outlet (D'Arcy Power, 1895; McFarland, 1911; Dwyer, 1944). Direct ureteric involvement, a well-recognized sequel of cancer of the cervix in adults, is exceptional in sarcoma botryoides of children; I have found mention of it only in the paper by Harding and Hankins (1937); Owen (1933), describes a fatal case with peritonitis and a right hydronephrosis, but gives no details of the cause of the obstruction.

Dissemination of the growth to the regional pelvic and para-aortic lymph-nodes has been reported by Bidone (1904), by Demme (1881), and by others, but this, too, seems to be relatively uncommon. Pleural and pulmonary metastases are recorded by Dugge (1930), by Nagel (1933), and by Willis (1948)—this type of spread occurring more frequently in adults than in children.

FIG. 29.—Operative specimen showing uterus, vagina filled with polypoid growth, and vulva. The bladder and right pubic ramus is on the reverse side of the specimen and is not visible. (*Actual size.*)

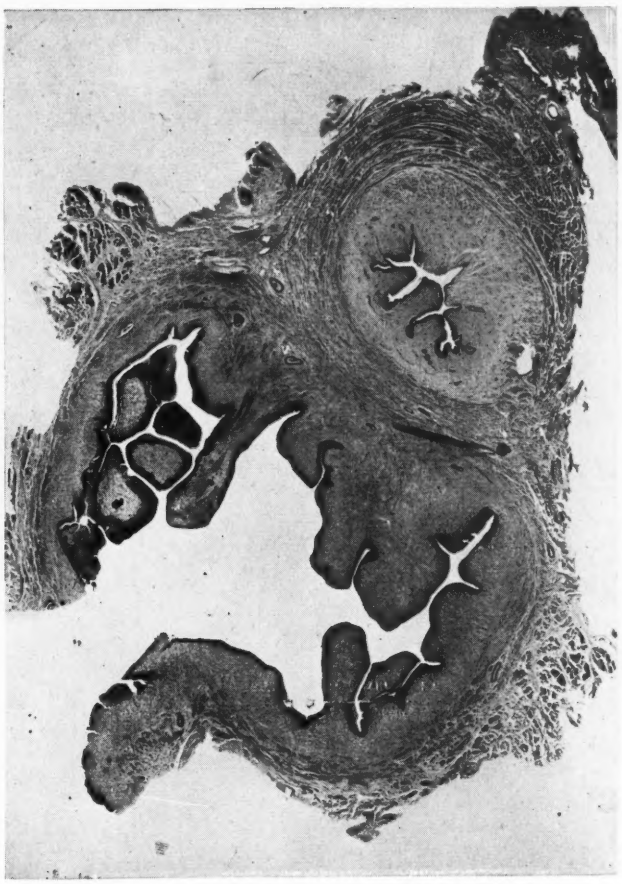

FIG. 30.—Microscopical appearance (low-power) showing polypoidal growths arising from vaginal wall. Uterus seen above and to the right is not involved.

Microscopically, sarcoma botryoides characteristically consists of an œdematous, myxomatous, or cellular stroma containing pleomorphic cells—some of which are large, and contain several nuclei, with striated fibrils in their cytoplasm. The term rhabdomyosarcoma is applied to the tumour and summarizes the histology. The large striated cells—and strange it is that striated cells are more common in tumours other than those of voluntary muscle (Foot, 1945)—lie adjacent to and mingled with actively-growing myeloblasts. Epithelial cells of the vaginal skin may cover the tumour and indent its surface; ulceration may be present. Bone and

cartilage have been described as an occasional occurrence (Willis, 1948).

Evolution of the Disease.—McFarland in his monumental paper (1935) does not give details of the outcome in the cases he collected. Glynn and Blair-Bell (1914) summarized the course of the disease in 15 cases out of 17 recorded in the literature

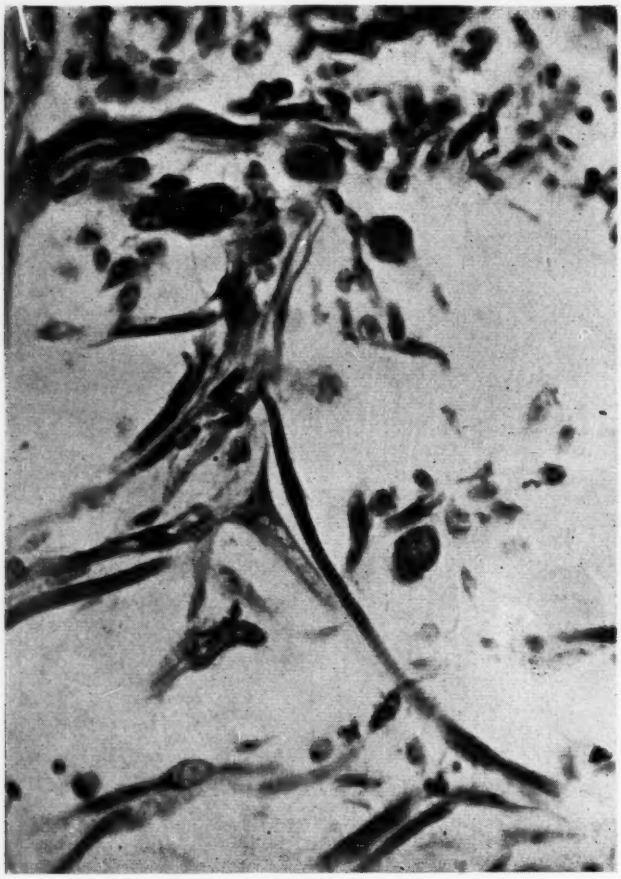

FIG. 31.—Microscopical appearance (high-power), showing striated cells and large myeloblasts.

up to that time, but quote only 2 examples of sarcoma botryoides in children. Adler (1928) was able to detail 37 examples in children out of a total of 42 recorded cases of the disease.

To make the list up to date there must now be added the following case reports: Shaw (1928), 1 case; Brumwell (1929), 1 case; Owen (1933), 1 case; McFarland (1935), 1 case; Novak and Anderson (1937), 2 cases; Harding and Hankins (1937), 1 case; Amolsch (1939), 1 case; Dwyer (1944), 1 case; Ulfelder and Quan (1947), 1 case; Fasanotti (1948), 2 cases; Willis (1948), 2 cases; and the case of the present author.

Thus there is now available for study at least 54 cases with details of the progress of the disease (*Table II*).

The table emphasizes the lethal power of the disease and confirms previous studies to this effect. Of the 54 children whose case records are available in the literature, only 5 appear to have survived for two years or more (Brumwell, 1929; Halle, Grisel and Veau, quoted by McFarland, 1935; Schurchardt, 1888; Demme 1881; Babes, quoted by Adler, 1928). The majority of the cases collected by Adler proved fatal within a short time of diagnosis or treatment, chiefly from local extension of the disease; in only 5 were distant metastases recorded at death.

Treatment.—From a study of the case reports to date it is clear that local operations are commonly followed by local recurrence of the growth, while spread by metastasis is comparatively rare. For

FIG. 32.—Radiograph showing extent of resection of pubis on right side.

this reason, if it be accepted as a general principle that any form of malignant disease is potentially curable by radical surgery provided the growth has not spread beyond the field of excision, the disease sarcoma botryoides should, theoretically at any rate, be amenable to cure in some cases.

With this concept in mind, it was decided to undertake surgical treatment in a child 4 years of age and to carry out excision of the vagina, uterus, bladder, and urethra, with transplantation of the ureters into the colon.

CASE REPORT

S. C., aged 4 years. Hospital number 72008.

January, 1947: Œdematous tags noticed to present from between the labia.

March: Biopsy under general anæsthesia. Histological diagnosis of sarcoma botryoides. (Dr. B. Lennox.)

May 1: Bilateral uretero-colic transplantation under general anæsthesia. No evidence of spread of disease to pelvic lymph-nodes.

May 5 : Bilateral nephrostomy under local anæsthesia for suppression of urine.

June 5 : Perineal resection of vulva, vagina, uterus, urethra, and bladder, together with the pubic ramus on the right side.

On June 5, 1949, 2½ years from the time she was first seen, the child appears well, attends school, and has complete urinary control. She has no nocturnal urination. Her gait is normal. There is no sign of persistence of the disease.

The photographs show the macroscopical (*Fig.* 29) and microscopical (*Figs.* 30, 31) appearances of the lesion, the radiograph (*Fig.* 32) shows the extent of resection of the pubis, and the clinical photographs (*Figs.* 33, 34) demonstrate the healed incision and the present appearance of the child.

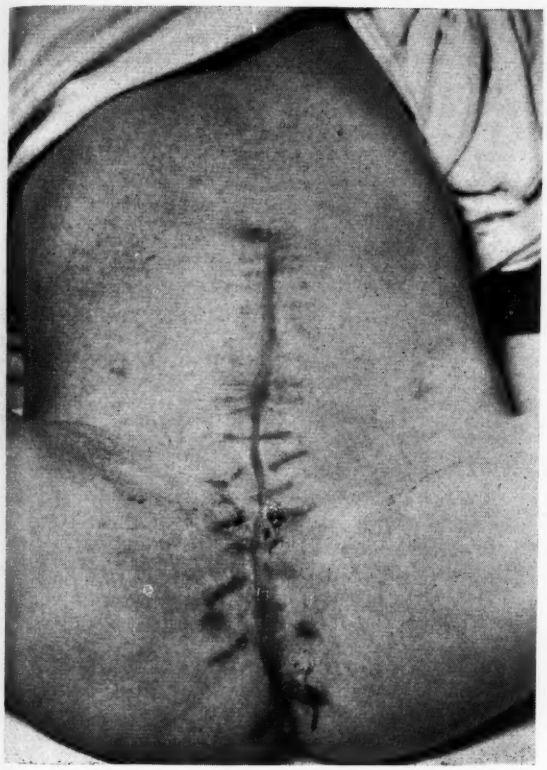

FIG. 33.—Clinical photograph showing extent of incision.

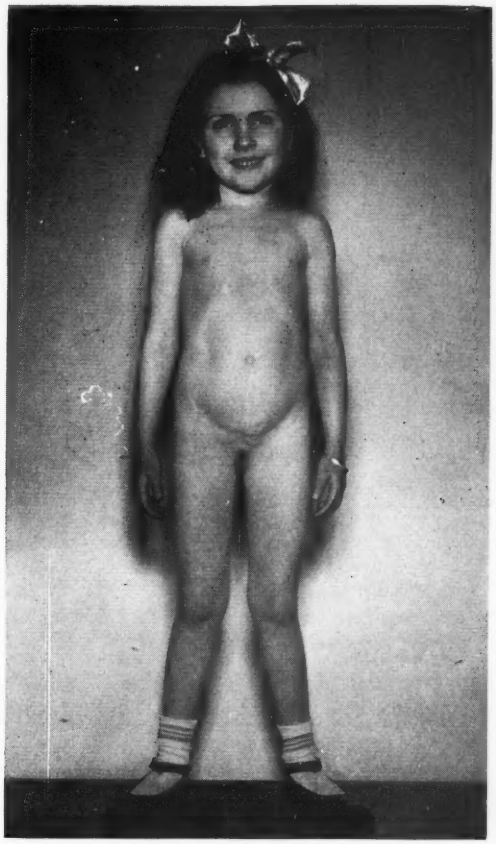

FIG. 34.—Clinical photograph of child 2½ years after she was first seen.

DISCUSSION

With the exception of the recent paper by Ulfelder and Quan (1947) the literature is devoid of any discussion of treatment of sarcoma botryoides in children. Local excision of the growth or X-ray therapy—as might be anticipated—are characterized as unsuccessful.

Some few continental surgeons (Schiller, 1894 ; Hollander, 1896 ; Amann, 1907 ; Grafenberg, 1912) long ago realized the possibility of radical surgical excision of the vagina and uterus, but their individual efforts went unrewarded. Three of the children so treated died within a few days of operation, while the fourth died " in a short time " with a recurrence. During the subsequent thirty-five years there is no recorded attempt at cure by surgical excision.

In 1947, Meigs (Ulfelder and Quan, 1947), of the Massachusetts General Hospital, operated upon the first case of sarcoma botryoides seen at that hospital. Familiar with the operation of Wertheim, he undertook a radical excision of the uterus and vagina through an abdominal approach, but found it necessary also to resort to a perineal excision of the vaginal stump, the transection of which had occurred during the abdominal procedure. But, even so, he was apparently successful and avoided the hazard of a urinary fistula consequent on sloughing of the ureters as a result of baring them. The potential reward of this type of operation is the patient with normal micturition, but Meigs's patient had to be catheterized for residual urine for three months.

In the same year, and without knowledge of Meigs's contemporaneous work, I operated on the child whose history is given above. Desirous of obtaining a wide excision of the parametrium and, at the same time, avoiding the risks involved in extensive dissection of both ureters, it was decided to sacrifice the natural mechanism of micturition. Once the ureters had been transplanted into the colon, extirpation of the vagina, uterus, urethra, and bladder was relatively simple—especially when the pubis had been excised.

It is still too early to talk of cure but the result to date would appear to justify optimism and to demonstrate the feasibility, even in very young children

of an operation which is admittedly radical, but which offers relief from so lethal a disease.

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THE VALUE OF THE FIBRINOGEN-B TEST IN INTRAVASCULAR THROMBOSIS IN SURGICAL SUBJECTS

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CUMMINE (1947, a) and Cummine and Lyons (1948) have proposed a method designed to determine whether a patient is or is not likely to develop venous thrombosis following operation. Such a determination designed to recognize the presence of the prethrombotic state, if successful, would be of extreme value. In this paper we have attempted to confirm their findings. We have also carried out tests on the clotting time in relation to temperature in these patients. We have further tried to determine if a certain prophylactic dose of heparin is of value in patients developing fibrinogen B and also if a smaller dose than is usually given is adequate where signs of thrombosis have developed.

Discussions were carried out with Dr. I. B. Jose, Director of Surgical Studies, University of Adelaide, and patients under his care at the Royal Adelaide Hospital were investigated in the above manner.

METHOD

Randomization.—A random series of 52 black and red colours were obtained (R, R, R, B, B, B, R, B, . . . B). As patients developed a positive fibrinogen B they were allotted in this order: R, untreated; B, treated. It was decided to test the blood of all patients belonging to the following groups: All prostatic cases, lower limb fractures, and lower abdominal (operative). The types of investigations were to be: Daily clotting times and a fibrinogen-B test every second day except immediately post-operatively, when it would be performed daily if the situation warranted it. We carried out the fibrinogen-B tests without knowing the name of the patient to whom the plasma belonged until the test was completed.

It soon became apparent that a very low clotting time was quite compatible with no symptoms or signs of thrombosis and for reasons to be given later the clotting time was not pursued after we were satisfied. Heparin was given in all cases where fibrinogen B appeared. This applied to patients in B group. Patients in R group received heparin only if in addition to the presence of fibrinogen B they developed one single definite symptom or sign of thrombosis.

Heparin Dosage.—The dosage of heparin given was as follows:—

Prophylactic (Group B without symptoms): 8000 U. (colorimetric unit) i.v., 12-hourly, maintained for five days, reducing the dose to 8000 U. on the fifth day when therapy discontinued.

Definite symptoms developed: Muscle deeply tender, slight temperature, etc. Immediately—8000 U. 8-hourly i.v. Third day reduced to 8000 U. 12-hourly, fifth day 8000 U. i.v. only, then discontinued.

* This work was aided by a grant from the National Health and Medical Research Council.

Gross thrombosis (phlegmasia): 9000 U. 8-hourly for 3 days, then 8000 U. 8-hourly for 4 days, then 8000 U. 12-hourly for 2 days, and finally 8000 U. on the tenth day.

Pulmonary infarct (embolism): Initially 9000 U. 6-hourly.

Fibrinogen-B Test.—4.5 ml. of blood was collected into a bottle containing 0·5 ml. of 1·1 per cent sodium oxalate. To 1 ml. of supernatant plasma six drops of reagent were added, the whole shaken, and readings made at 5 minutes. Readings were made as outlined by Lyons (1945) (Cummine and Lyons, 1948), and ± = a trace.

Fibrinogen-B Reagent (*Lyons*, 1905).—10 g. β-naphthol dissolved in 500 ml. of ethyl alcohol, made up to 1000 ml. with distilled water. Oxygenated for two days until the solution turned brown, kept in stoppered bottle.

Clotting Time (*Kolmer and Boerner*, 1938).—The finger was cleansed and punctured as for a blood-count, and the procedure followed except that readings were begun at 1 minute. In some instances these were carried out at room temperature.

EXPERIMENTAL

In this series 108 patients were investigated. Of these at some stage following operation or injury by fracture, 53 developed a positive reaction to the fibrinogen-B test (*see Table I*). Of these, 7 contained a trace only of fibrinogen B in the plasma, 24 developed + (maximum), 18 ++ (maximum), and 4 +++ (maximum).

Venous Thrombosis.—Of the 53, 9 patients developed symptoms or signs of thrombosis (*see Table I*), of which 4 were in the group allotted for treatment with heparin prophylaxis since they developed a positive fibrinogen-B test (one of these had symptoms which were doubtful) and were lettered B. In all instances the symptoms developed a few hours before the heparin was given. In no instance did further signs or symptoms of thrombosis develop in these patients while prophylactic treatment was given. In two instances, after 14 days' and one day's cessation of heparin treatment respectively, symptoms recurred, and following a further treatment with heparin of the same schedule there was no further recurrence. One, however, later developed fibrinogen B and further treatment with heparin was given. Now in one instance (*Case* 68) one patient in the treated group with a positive fibrinogen B developed thoracic signs and symptoms possibly due to an embolus (but more probably due to pneumonia) before symptoms of the thrombosis and also before heparin was given. Symptoms disappeared while heparin was given. This case was doubtful.

In 5 instances signs and symptoms of thrombosis developed in patients allotted as not for treatment if they developed a positive fibrinogen B, which they did. Of these, 4 were not given treatment and no further symptoms developed. One of these patients was definitely a case where we considered there was thrombosis: the remaining three were doubtful. The fifth subject developed an embolus, was treated with heparin for eight days and then developed symptoms of thrombosis three days later with embolism. Heparin was given for a further eight days with recovery.

Pulmonary Embolism.—In 1 instance a patient developed a probable embolus without signs of thrombosis in the group set aside for treatment with heparin and symptoms developed before heparin was given, but following treatment with heparin no further symptoms developed. Later this subject developed positive fibrinogen B after cessation of treatment and a further course of heparin was given and no symptoms developed. No patient developed embolus without signs of thrombosis in the 'no-treatment' group.

Of the patients who remained negative to the fibrinogen-B test throughout, 4 developed signs of thrombosis. Of these, 3 were cases of doubtful thrombosis. One patient of these 3 developed symptoms which might have been due to embolism but we consider were possibly due to pneumonia. This will be amplified later. Three further patients developed signs of embolism without thrombosis; of these, 1 case, which we considered definitely was a case of embolus, was not considered sufficiently ill to cause any anxiety and so was not given heparin. In the remaining 2 instances it was considered that the diagnosis was possibly embolism and this will be amplified later.

a. Patients who developed Signs or Symptoms of Pulmonary Infarct or Venous Thrombosis, in whom Fibrinogen B was Present.—

Case 68.—I. O'L., female, aged 87. *Pertrochanteric fracture left femur, treated in a Thomas splint with skeletal traction by Kirschner wire through the upper end of the tibia.* This patient developed a mild pyrexia and signs at the base of the left lung one month after admission. This was followed within a week by signs at the base of the right lung. No signs of peripheral thrombosis developed but fibrinogen B appeared (+). The patient was given chemotherapy and a prophylactic course of heparin with resolution of signs and symptoms. Two months after admission she developed slight pain and tenderness of the right calf with fibrinogen B +. A prophylactic course of heparin was given with subsidence of symptoms and signs. One month after cessation of this course of heparin she developed a fibrinogen-B ±, but with no signs or symptoms. Prophylactic heparin was given again with no further developments.

Comment.—While clinically we considered the patient had developed pneumonia, we have designated this as a case of ' ? pulmonary infarction ' in *Table I*, so

Table I.—INCIDENCE OF FIBRINOGEN B, THROMBOSIS, AND EMBOLISM

FIBRINOGEN B	POSITIVE		NEGATIVE
Number of patients	53		55
Treatment	'Prophylactic' treatment	No treatment	No treatment
Number of patients	26	27	55
Developed signs of venous thrombosis only	3	4 (? 3)	3 (? 2)
Developed signs of pulmonary infarct and venous thrombosis	1 (? 1) (thrombosis ?)	1 (thrombosis definite)	1 (? 1) (thrombosis definite)
Developed signs of pulmonary infarct without venous thrombosis	1 (? 1)	—	3 (? 2)

that the table may be completely inclusive of all possible cases. It is probable, but not certain, that the patient had a venous thrombosis, and this is designated ' thrombosis ? ' in the table.

Case 69.—R. O., female, aged 82. *Fractured neck of left femur with insertion of Smith-Petersen pin three days after admission.* Two days after operation she developed pain and tenderness in both calves and a positive Homan's sign in the right calf. Fibrinogen B was negative until five days later, when she still had the same symptoms but with fibrinogen B ++. Next day the tenderness had extended to her right thigh and slight œdema was present. The heparin, which was commenced also on this day, was given for ten days—' phlegmasia ' dosage with gradual subsidence of signs and symptoms. A further fibrinogen B + was obtained three weeks after cessation of the heparin course. No further heparin was given (temporary lack of supplies) and no further signs or symptoms developed. She was discharged to a convalescent ward.

Comment.—This was considered a definite case of venous thrombosis.

Case 70.—The same patient as *Case* 69 readmitted three weeks after discharge with *acute intestinal obstruction and subjected to laparotomy*, with division of adhesions not causing any obstruction to the great veins. No signs or symptoms referable to her previous thrombosis were present. Fibrinogen B + developed the day after laparotomy and was negative the next day, but with no signs or symptoms of thrombosis. Prophylactic heparin was not commenced until the third day because of the danger of post-operative hæmorrhage. The day after cessation of prophylactic heparin she developed soreness in both calves with fibrinogen B negative and no signs. Next day the fibrinogen B was again negative but the left calf was tender and there was slight œdema of the ankle. Next day the left calf was very tender. Homan's sign was positive and slight œdema was present and heparin was commenced. The clotting times for the three days during which the patient was unheparinized and in which these symptoms developed were, at 37° C., 3½, 2, and 2 minutes, and at room temperature, 7, 6, and 10 minutes. No further recurrence of signs or symptoms followed this course of heparin. These findings are shown in *Fig.* 35, where the clotting time, the time of onset of symptoms, and the period of heparinization are shown.

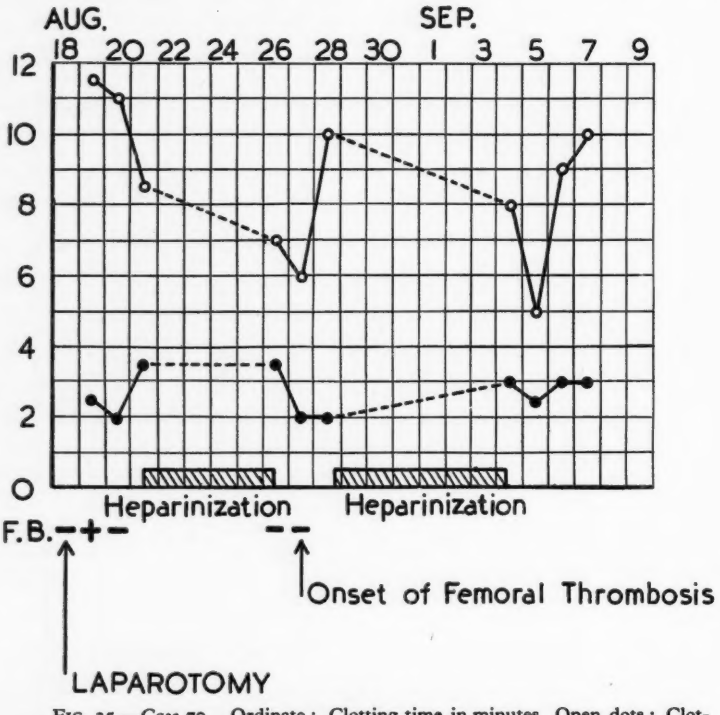

FIG. 35.—*Case* 70. Ordinate: Clotting time in minutes. Open dots: Clotting time at room temperature. Closed dots: Clotting time at 37° C. Abscissa: Date. Heparinization and onset of femoral thrombosis indicated. F.B.: Fibrinogen-B test results. (For details, *see* text.)

Comment.—This is regarded as a definite case of venous thrombosis.

Case 102.—E. W., female, aged 58. *Infected sinus following perineal resection of rectum.* Eleven days after admission this patient developed a tender right calf and a positive Homan's sign with a fibrinogen B +. The clotting time was 2½ minutes at 37° C. and 11 minutes at room temperature. A course of heparin treatment was given as for phlegmasia, with subsidence of signs and symptoms.

Comment.—This is regarded as a definite case of venous thrombosis.

Case 67.—A. O., female, aged 70. *Pertrochanteric fracture of femur treated in a Thomas splint with Kirschner wire through the upper end of the tibia.* This patient developed sudden pleuritic pain in the chest four days after admission. There were no signs of lung consolidation. The fibrinogen-B test was +. No signs or symptoms were present in the legs. She was given a heparin course for " likely thrombosis " with complete disappearance of symptoms. The fibrinogen-B test was + again two days after the heparin course without signs or symptoms. A further course of heparin was given. No further signs or symptoms developed.

Comment.—We are not confident that this patient developed an embolus from a venous thrombosis. It might be a case of fat embolism. It is just possible it is a case of pulmonary venous thrombosis. We cannot feel confident that it was a case of pleurisy or pneumonia and there was no friction rub. Designated ' ? pulmonary infarct ' (without venous thrombosis) in *Table I.*

Case 3.—B. A., male, aged 65. *Carcinoma of prostate. Bilateral orchidectomy.* Two days after operation he complained of a pain in the upper part of the left thigh and the fibrinogen-B test was +. Next day pain and slight tenderness were present in the left calf. These symptoms and signs subsided within two days, and although the fibrinogen-B test was + on three further occasions within the week nothing more was observed suggesting thrombosis or embolism. This patient was untreated (belonging to Group R). The clotting time (37° C.) pre-operatively was 3 minutes and daily post-operatively (37° C.), 4½, 2, 5, 5, 5, 2½, 2½, 1½, and 3 minutes.

Comment.—While this may be a case of venous thrombosis, we are not certain. Designated ' ? venous thrombosis ' in *Table I.*

Case 22.—F. E., male, aged 66. *Millin's prostatectomy.* The fibrinogen-B test was + the day following operation and negative the second post-operative day. The night of the third post-operative day he developed sudden pleuritic pain, dyspnœa, and cyanosis. The fibrinogen-B test was + the next morning and pulmonary symptoms were still present, although no signs were present in the legs. He was regarded as a fairly definite

case of pulmonary infarction. Since this patient was in Group R, as soon as his clinical condition warranted it, two days after the onset of symptoms a course of heparin (as for ' phlegmasia ') was given for eight days. Three

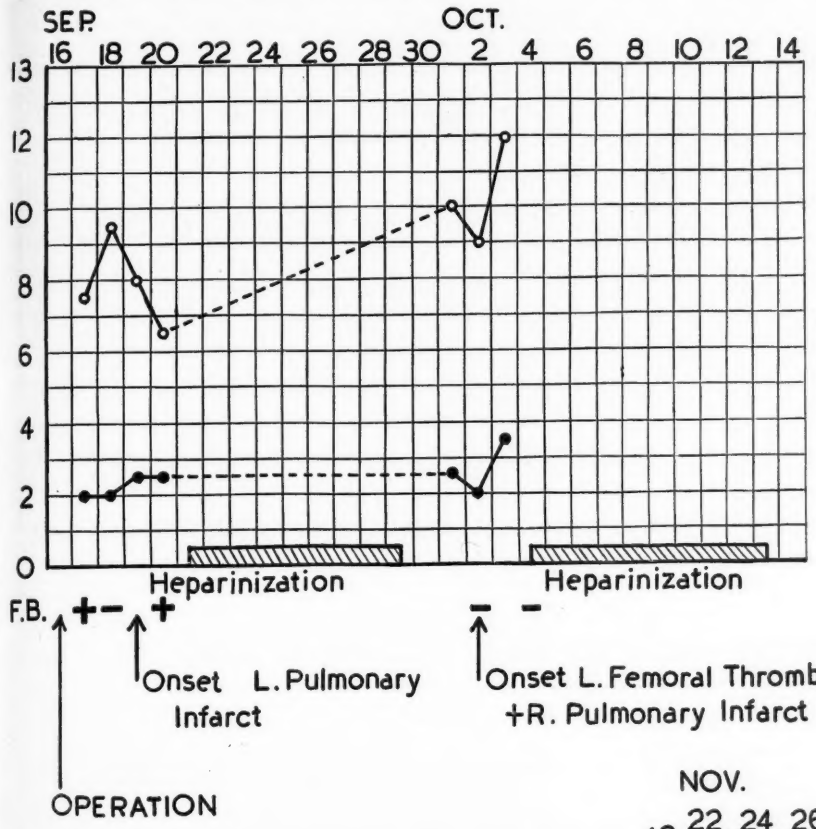

FIG. 36.—*Case* 22. Ordinate: Clotting time in minutes. Open dots: Clotting time at room temperature. Closed dots: Clotting time at 37° C. Abscissa: Date. Heparinization and onset of pulmonary infarct and femoral thrombosis indicated. F.B.: Fibrinogen-B test results. (For details, *see* text.)

days after the cessation of heparin with a negative fibrinogen B he again had pain in the other side of the chest and also a painful left calf. He was given another course of heparin for eight days with resolution of symptoms and signs and he had no further recurrence. His daily clotting times before the first course of heparin were 2, 2, and 2½ at 37° C. and 7½, 9½, and 6½ at room temperature, and before the next course of heparin were 2½, 2, and 3½ minutes at 37° C. and 10, 9, and 12 minutes at room temperature. These findings are shown in *Fig.* 36.

Comment.—This was regarded as a definite case of venous thrombosis and embolism.

Case 75.—A. P., female, aged 78. *Senile gangrene of the right foot. Below-knee amputation of the right leg.* On the third day after operation the fibrinogen-B test was ++ and her left calf was noticed to be apparently tender the next day. On the fifth day the fibrinogen-B test was again ++ and on this day a course of heparin was begun. Her thrombotic signs did not progress, but she developed a typical bilateral pneumonia with râles and consolidation on the eighteenth day and died on the twenty-third day. She was unco-operative and demented all the time.

Comment.—It is considered that the patient probably had a venous thrombosis, but we are not certain. This patient is designated ' ? venous thrombosis ' in *Table 1*.

Case 107.—E. V., male, aged 67. *Carcinoma of the prostate with endoscopic resection.* The fibrinogen-B test was + on the first post-operative day and thereafter became negative until discharge. On the second post-operative day he had pain and tenderness in the right calf which persisted and was accompanied by similar findings in the left calf on the seventh day. No œdema developed at all and no heparin was given. He became ambulant and was discharged without any complications.

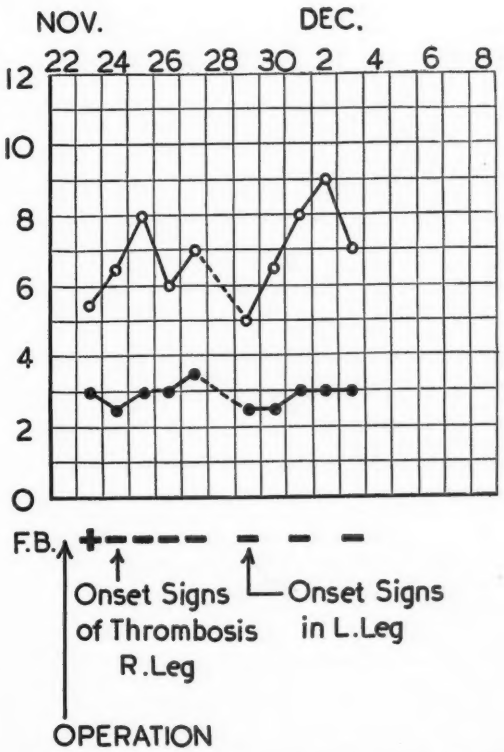

FIG. 37.—*Case* 107. Ordinate: Clotting time in minutes. Open dots: Clotting time at room temperature. Closed dots: Clotting time at 37° C. Abscissa: Date. Onset of signs of thrombosis indicated. F.B.: Fibrinogen-B test results. (For details, *see* text.)

His clotting time at 37° C. remained between 2½ and 3½ minutes constantly and at room temperature varied from 5 to 9 minutes. These findings are shown in *Fig.* 37.

Comment.—We have regarded this case as one of venous thrombosis.

Case 85.—S. S., male, aged 70. *Endoscopic resection of prostate.* The fibrinogen-B test was + on the second post-operative day and was negative thereafter until discharge, but no signs or symptoms developed until the thirteenth day when he complained of painful calves. His right calf was tender and Homan's sign was negative and his left calf was somewhat less tender. This settled down within four days, when he became ambulant and was soon discharged. He received no heparin.

Comment.—This may be a case of venous thrombosis but we are not certain. This patient is designated '? venous thrombosis' in *Table I.*

b. Patients who developed Signs or Symptoms of Pulmonary Infarct or Venous Thrombosis, in whom Fibrinogen B was absent.—

Case 1.—R. A., female, aged 58. *Strangulated left femoral hernia.* At operation her left femoral vein was damaged and had to be repaired, and no certainty was expressed as to the amount of venous lumen (if any) remaining. For this reason the signs which developed in this leg are not regarded as a true post-operative thrombosis. On the eighth day she had a tender left calf and slight œdema of the leg and the tenderness had extended to the thigh by the eleventh day and slight œdema was still present. This gradually subsided and she remained fibrinogen-B negative throughout and her clotting time remained constant at 5 to 5½ minutes at 37° C. except for one reading of 3½ minutes towards the end. This patient received no heparin.

Comment.—While this may be a case of venous thrombosis, we cannot be at all confident in including this with venous thrombosis. This patient is designated '? venous thrombosis' in *Table I.*

Case 36.—W. G., male, aged 71. *Subtrochanteric fracture of the right femur treated by skeletal traction in a Thomas splint and after ten days by an intramedullary pin.* The fibrinogen-B test remained negative consistently. His clotting time at 37° C. varied between 2½ and 4 minutes throughout. On the sixth day he developed pain and tenderness in the right calf, with Homan's sign positive on the eighth day. This pain and tenderness subsided by the eleventh day, which was his first post-operative day. Five weeks after admission he developed soreness in the left chest and consolidation at the right base. His X-ray of the chest nine weeks after admission showed chronic fibrotic lesions of both lungs, mainly the upper zones with some basal pleural thickening.

Comment.—We regard the original limb condition as a definite venous thrombosis. Though we consider his thoracic symptoms and signs were probably pneumonic, so that the table may be completely inclusive of all possible cases, we have designated this as '? pulmonary infarct' in *Table I.*

Case 94.—T. T., male, aged 72. *Fractured left tibia and fibula treated in a full leg plaster in a Thomas splint with skeletal traction through os calcis.* He remained negative to the fibrinogen-B test throughout. On the twentieth day he complained of pain in the right calf, which was very tender. Homan's sign was negative. The pain remained for one week, gradually subsiding. He received no heparin. He was discharged well, but still in plaster, after 4½ weeks.

Comment.—This was regarded as probably a case of thrombosis, but as we are not certain it has been designated '? venous thrombosis' in the table.

Case 104.—E. W., female, aged 78. *Intestinal obstruction. Cæcostomy.* On the second post-operative day she developed a tender left calf and slight œdema of the ankle. The next day the tenderness was still present and extending up the thigh and definite œdema was present. She was given a course of heparin for ten days with

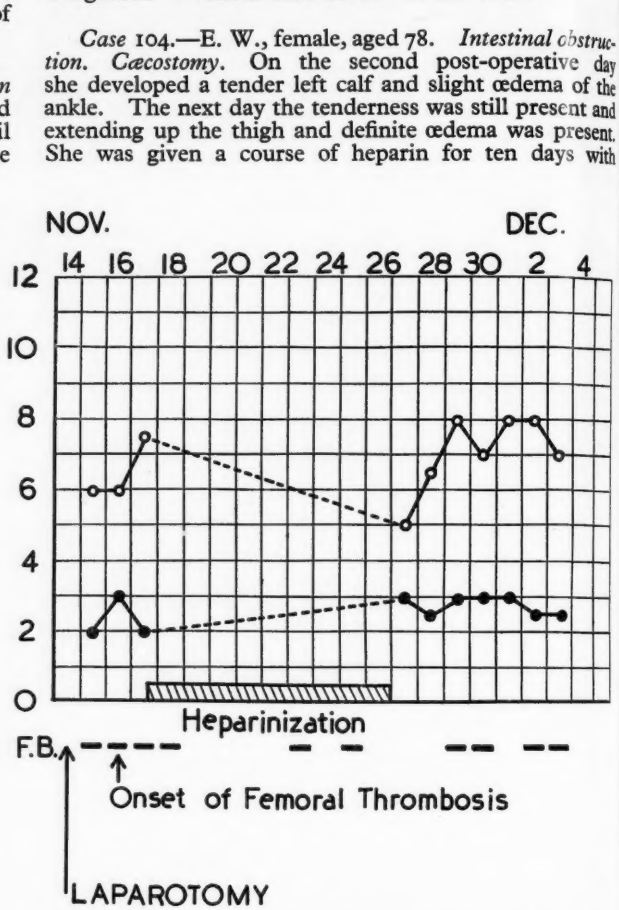

FIG. 38.—*Case* 104. Ordinate: Clotting time in minutes. Open dots: Clotting time at room temperature. Closed dots: Clotting time at 37° C. Abscissa: Date. Heparinization and onset of femoral thrombosis indicated. F.B.: Fibrinogen-B test results. (For details, *see* text.)

gradual subsidence of symptoms, although the œdema was slow to disappear. Her blood was negative to the fibrinogen-B test throughout, and the daily clotting times prior to heparinization were 2, 3, and 2 minutes at 37° C. and 6, 6, and 7½ minutes at room temperature.

Comment.—This patient was regarded as a definite case of venous thrombosis clinically. These findings are shown in *Fig.* 38.

Case 26.—A. F., female, aged 65. *Pertrochanteric fracture of the left femur. Skeletal traction in Thomas splint.* On the fifth day she developed pain in the right side of the chest with slight pyrexia. No physical signs were present. (? Thrombosis or fat embolism.) Her plasma was negative to the fibrinogen-B test throughout, and daily clotting times varied between 2 and 3 minutes at 37° C. and 5 and 10 minutes at room temperature.

Comment.—This may have been a case of pulmonary thrombosis as distinct from embolus, but we are not certain that the condition is due to thrombosis either in limbs or lungs. This patient is designated '? pulmonary infarct without venous thrombosis' in *Table I.*

Case 78.—T. R., male, aged 58. *Compound fracture right tibia and fibula.* He developed slightly blood-stained sputum seventeen days after admission. He also complained of a pain in the right side of his chest, which he said had been present from the time of the accident

but was now a little worse. The legs presented no signs or symptoms of thrombosis. His cough was not any worse than usual (heavy smoker). He was not pyrexial. His plasma was negative to the fibrinogen-B test. An X-ray examination of the chest was negative.

Comment.—His symptoms were regarded as possibly due to pulmonary infarction, but in view of the history we cannot exclude the role of trauma. No evidence of tuberculous infection was discovered. No heparin treatment was given and he gradually settled down. This patient is designated '? pulmonary infarct without venous thrombosis' in *Table I*.

Case 95.—H. W., male, aged 35. *Compound fracture left tibia and fibula, treated with skeletal traction in a Thomas splint.* Twenty-three days after admission he developed a sudden pleuritic pain in the right side of the chest with a cough. He developed a pyrexia to 100° F. the next day. He was regarded clinically as a case of pulmonary infarction. As his general condition was quite good and clinical observation was desired, heparin was withheld. His chest signs and symptoms gradually resolved without further incident. His plasma was negative to the fibrinogen-B test on each occasion.

Comment.—This case was regarded as one of pulmonary infarction.

The clotting times of many patients in the series were also investigated. As described above, this was done at constant temperature, as it is recognized

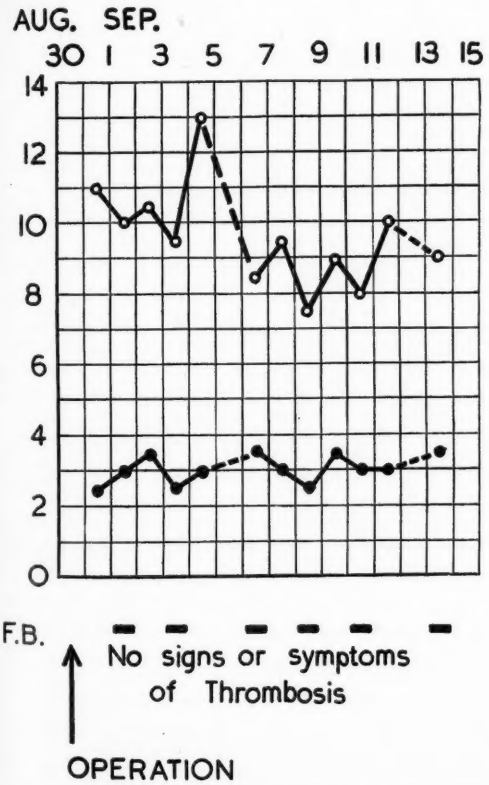

FIG. 39.—*Case* 20. I. D., male, aged 18. Carcinoma of rectum. Abdomino-perineal resection. Comparison of clotting times at room temperature and 37° C. Ordinate: Clotting time in minutes. Open dots: Clotting time at room temperature. Closed dots: Clotting time at 37° C. Abscissa: Date. Fibrinogen-B response negative throughout. No signs or symptoms of thrombosis. (*See* text.)

physiologically that such a reaction is subject to temperature influence in its rate of accomplishment. The results obtained justified this opinion. Of a total of 528 readings at constant temperature (37° C.), no less than 459 readings were between 2 and 4 minutes (*Table II*), and furthermore, in the case of

Table II.—RESULTS OF CLOTTING TIMES (37° C.)

	No. of Readings
6 minutes and over	0
5 " " "	10
4 " " "	52
3 " " "	235
2 " " "	224
1 minute " "	7
Total number of readings	528

individual patients, it was found that the clotting times did not vary markedly if read at a constant temperature. As this became clear from the results

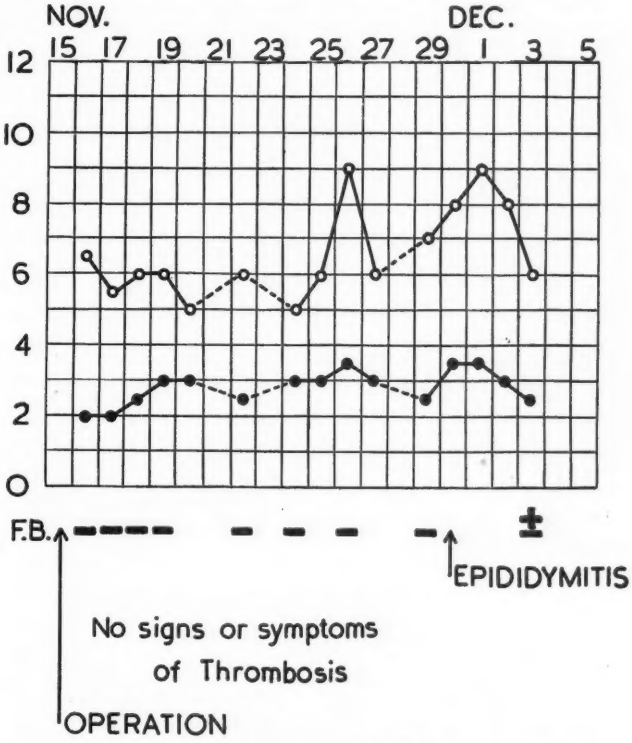

FIG. 40.—*Case* 108. T. V., male, aged 68. S.P. prostatectomy. Comparison of clotting times at 37° C. and room temperature. Ordinate: Clotting time in minutes. Open dots: Clotting time at room temperature. Closed dots: Clotting time at 37° C. Abscissa: Date. F.B.: Response to fibrinogen-B test indicated. At second arrow onset of epididymitis. No signs or symptoms of thrombosis. (*See* text.)

obtained, it was decided to test the clotting times of some patients using simultaneous readings at 37° C. and at room temperature. Twenty-two patients were tested in this way with uniform findings of a relatively constant reading at 37° C. with limits of 1½ to 5½ minutes (average 2·9) and simultaneous readings at room temperature varied daily between the limits of 4½ minutes and 15 minutes (average 7·7). The average clotting time of patients who developed thrombosis was 3·2 minutes at 37° C. and 8·7 minutes at room temperature. These findings are indicated in *Figs.* 39 and 40. In *Fig.* 39 it is noted that the clotting times at 37° C. were consecutively 2½, 3, 3½, 2½, 3, 3½, 3, 2½, 3½,

3, 3, and 3½ minutes, while at room temperature it was 11, 10, 10½, 9½, 13, 8½, 9½, 7½, 9, 8, 10, and 9 minutes respectively. A difference in results was quite noticeable if the capillary tube was held in the hand or put on a cloth or on a metal table top.

DISCUSSION

It is evident that it is quite compatible whether fibrinogen B be present in the blood or not to have signs of venous thrombosis or pulmonary infarction develop. In 53 patients in whom the fibrinogen-B test was found to be positive in the blood, definite signs of venous thrombosis developed in 5 instances (plus a further 4 doubtful ones) and pulmonary infarction developed in 1 (plus a further 2 doubtful ones). In 55 instances in which the fibrinogen-B test was negative in the blood, venous thrombosis developed in 2 (with a further 2 in which there was some doubt in the diagnosis) and pulmonary infarction developed in 1, and also in a further 3 it was doubtful. These patients were situated in a surgical ward and had been operated on for some surgical condition affecting an organ below the level of the umbilicus or had a lower limb fracture.

If we regard all the cases as definite, 3 developed infarction in the positive series and 4 in the negative, while 9 developed thrombosis in the positive series and 4 in the negative. There may be some bias in favour of the development of venous thrombosis in patients who developed a positive fibrinogen-B test, but in view of the exceedingly high incidence of positive tests for fibrinogen B in the blood (almost half our cases) it seems that the test, even if it convincingly distinguishes the patients who would not develop thrombosis by a negative reaction, loses considerably in practical value, for then half the cases would require anticoagulants prophylactically. This shows a lack of specific relationship between a positive fibrinogen-B test and the development of intravascular thrombosis, and hence it is not a reliable guide in the institution of anticoagulant therapy. Further, in our series where thrombosis developed in the positive fibrinogen-B group it occurred within a few hours of the development of the fibrinogen B and before heparin was able to be instituted in a number of instances. In these no further symptoms of thrombosis developed while heparin was given. Further Lyons has shown that fibrinogen B occurs in the blood in a very considerable number of conditions (Dunn, Jackson, and Lyons, 1949). This itself should indicate that the practical value of the test as a diagnostic of the development of venous thrombosis is greatly weakened. While the pursuit of such an aid should be continued vigorously, from our findings we are unable to support the use of the fibrinogen-B test as of any particular practical value.

Thus far we have discussed the occurrence of both a positive fibrinogen-B test and clinical signs of thrombosis or embolism in a patient without remarking on the times of their appearance. Clearly the fibrinogen-B test to have practical value in diagnosing the ' prethrombotic state ' should preferably show a positive reaction a few days prior to the onset of the thrombosis. Analysing the 9 cases of venous thrombosis (including 4 doubtful cases) among the 53 cases who showed a positive reaction to the fibrinogen-B test, we find that in 2 instances (*Cases* 75 and 107) the fibrinogen-B test was positive within the few days prior to the onset of thrombosis; in 3 instances (*Cases* 3, 68, and 102) it occurred the same day, and in 1 case (*Case* 69) it was not positive until after the development of thrombosis. In 1 case (*Case* 70) the fibrinogen-B test was positive one week prior to the development of the thrombosis and a five-day prophylactic course of heparin had also been given in this period. In another instance (*Case* 85) it was positive twelve days prior to the onset of the thrombosis. In another case (*Case* 22) it was positive twelve days prior to the onset of the signs of thrombosis but a pulmonary embolus (? thrombosis) and an eight-day course of heparin treatment preceded the development of the venous thrombosis.

Analysing the 3 cases (including 2 doubtful cases) of pulmonary embolism which showed a positive reaction to the fibrinogen-B test, we find that in 1 instance (*Case* 22) it was positive on two occasions within the few days preceding the signs of pulmonary embolism. In 1 instance (*Case* 67) it was positive the day following signs of embolism, and in the third (a doubtful case, *Case* 68) it was positive several days after the pulmonary signs.

In general whether heparin was used or not a positive response to the fibrinogen-B test of the blood was not found to be maintained for very long, which further weakens the importance of the test unless daily readings are carried out.

It has been suggested that an evaluation of the clotting times is of value in the diagnosis of imminent thrombosis. Bergquist (1940) has regarded a clotting time of three minutes as a danger level. Cummine (1947, a, b) has carried out extensive observations on the clotting times of the blood of patients and agrees with this thesis and particularly emphasizes the importance of a " fixation " of the clotting time and while there is typical fluctuation he is not worried. On the other hand, Cummine usually carries out the test at room temperature. We cannot agree that in practice this is satisfactory. Our reason for stating this is that we obtained very wide variations in the clotting times when they were carried out at room temperature compared with those at 37° C. This occurs when the same person carries out the test. Temperature variation and fluctuation is so considerable in various parts of Australia that it would be unreasonable to expect such an estimation to be satisfactory. The fallacy of testing the clotting time at room temperature is shown by the fact that when the test is carried out at room temperature and at 37° C. concurrently, the time is much slower and more variable at room temperature (*Fig.* 39). For another example, in 1 instance the clotting time was 5½ minutes at room temperature and 3 minutes at 37° C. On another occasion the clotting times were 9 and 3 minutes respectively. This patient developed thrombosis when the clotting time was 2½ minutes at 37° C. on 2 occasions (*Fig.* 37). In another instance when the clotting time was 2 minutes at 37° C. no signs or symptoms of thrombosis developed. Also we found generally no greater diminution of clotting time in the presence of imminent thrombosis than without. Actually the average clotting time of all patients whose blood was tested

at room temperature was 7½ minutes and at 37° C. a little less than 3 minutes, while in those who developed thrombosis, including the doubtful ones, the figures averaged 8½ minutes at room temperature and 3 minutes at 37° C. before thrombosis and 8 minutes (R.T.) and 3 minutes (37° C.) after thrombosis—that is, the clotting times were a little slower in those patients who developed thrombosis.

Therefore both on practical and theoretical grounds we are unable to support the value of the test as carried out. We find that when the clotting time is carried out under standard conditions there is very little difference in the readings, especially for each patient in repetition. Of 528 clotting times 459 were between 2 and 3½ minutes. This is the danger level of Bergquist (1940) and Cummine (1947, a). Presumably one would have to lower the danger level since we carried out the tests at 37° C. It seems without foundation to suggest that the speed in which blood clots *in vitro* should be closely related to spontaneous clotting of blood in a vessel. In the one instance we are concerned with the inherent capacity of the blood to clot under certain conditions; in the other we do not really know what factors operate in initiating the clot. Until we do, such an operation in the absence of empirical correlation can only be regarded as theoretical. The value of heparin in the treatment does not necessarily support the contention that a fast clotting time should be a danger signal, because heparin has a physiological effect upon the clot itself apart from speed of coagulation (Loewe, Hirsch, Grayzel, and Kashdan, 1948). Finally, from the practical point of view, we obtained no significant evidence that a rapid clotting time indicated a liability to develop thrombosis. In fact rapid clotting times were just as common in patients who did not develop thrombosis as in those who did.

It is to be recognized that in many instances the diagnosis of a minor pulmonary embolus must, as yet, remain a matter for conjecture. We have endeavoured in this paper to distinguish the definite cases of venous thrombosis and pulmonary infarction from the doubtful, and while we believe that the cases we have diagnosed as thrombosis or infarction definitely were, and that the doubtful cases may or may not have been, such conditions, this introduces a definite difficulty into the assessment both of the value of prophylactic treatment as a safeguard against the development of thrombosis and the significance of any test designed to distinguish those patients who will develop thrombosis. The clinical diagnosis of early venous thrombosis is not always clear-cut, as is seen from our series, but at present it probably provides the most reliable indication for the definite need of anticoagulant therapy.

SUMMARY

Investigations to determine the presence of fibrinogen B in patients in a surgical ward have been carried out.

In approximately 50 per cent of cases this test proved positive.

Of the patients developing positive fibrinogen B, half were given a prophylactic course of heparin.

Symptoms and signs of venous thrombosis and pulmonary infarction developed both in the fibrinogen-B positive and fibrinogen-B negative group.

No untoward symptoms developed in the patients who were given prophylactic heparin after treatment was instituted, though some had developed symptoms or signs of thrombosis or infarction immediately prior to the administration of heparin.

Clotting times of the blood of patients were estimated at 37° C. and at room temperature in many instances. No significant help as to the imminence of thrombosis was rendered from this investigation.

It was concluded that estimation of the fibrinogen B was not of any particular practical value.

In the instances recorded we found that a smaller dose of heparin than that usually advised, especially with regard to the frequency of dosage, was satisfactory in cases of embolism and thrombosis.

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RENAL HYDATID DISEASE

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HYATID disease of the kidney is a very rare condition. The total number of cases of hydatid disease recorded in the Louis Barnett Hydatid Registry of the Royal Australasian College of Surgeons is 2002, and of these only 44 are examples of renal cysts. The records of the Royal Prince Alfred Hospital, Sydney, compiled since the year 1900, contain 16 examples of renal hydatid disease. Gordon Craig and R. K. Lee-Brown, of Sydney, in 1928 were able to collect and record 16 personal cases of this disease, accumulated over a period of fifteen years' urological practice, this being the largest personal series recorded in the world literature at that time. It is therefore a malady that is met only once or twice in the course of a surgical lifetime.

The rarity of renal hydatid disease and the fact that hydatid disease in general may masquerade under a variety of clinical misdiagnoses prompts the writer to record the following five examples of renal cysts.

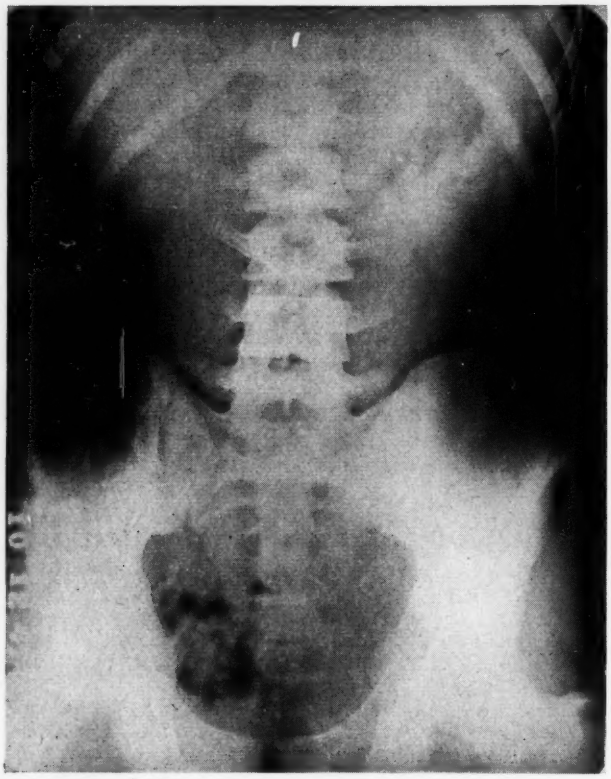

FIG. 41.—*Case* 1. A plain radiograph of the abdomen. Three small, rounded, calcific shadows are seen to lie in the approximate position of the left renal pelvis. The left kidney shadow is enlarged.

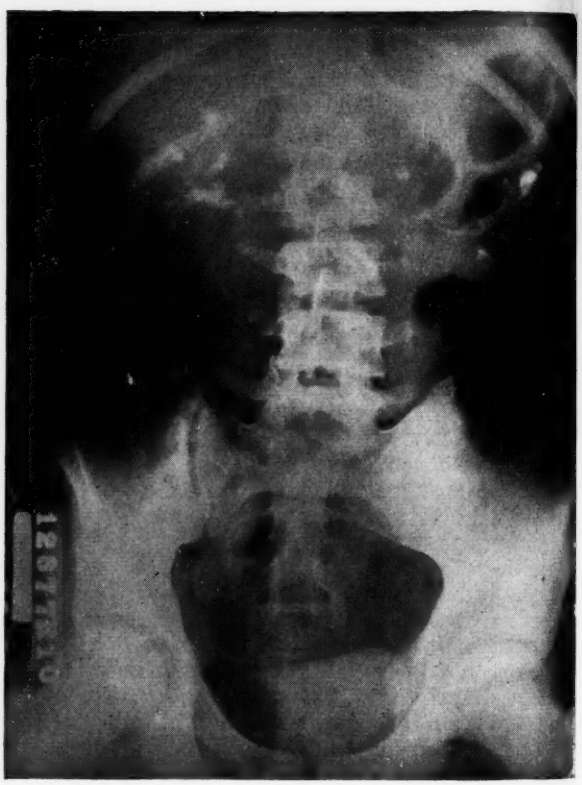

FIG. 42.—*Case* 1. An intravenous urogram. Both kidneys show good function but the upper and middle calices of the left kidney show elongation and distortion.

CASE REPORTS

Case 1.—An apparently healthy well-built muscular youth, aged 15 years, was admitted to hospital complaining of left-sided abdominal pain of ten months' duration. The pain was described as a dull uncomfortable feeling, which the patient referred to the left lumbar region. This had not been present continuously and was quite often absent altogether.

He had not noticed hæmaturia, nor had he passed any urinary calculi. For the past eight months he had noticed some frequency of micturition, about eight times daily, and had to rise once at night to pass urine. His urine had been scalding him for the past three months.

The patient's general health was good, his weight gaining, and there were no other symptoms.

The patient had lived in Sydney all his life except for a short holiday at Wollongong (about 50 miles south of Sydney) ten years ago. When 5 years of age he had kept a dog as a pet for about a year. The patient had had no previous illnesses or operations.

The only abnormal feature detected on physical examination of the patient was that deep pressure in the left costovertebral angle elicited tenderness.

ON EXAMINATION.—Urine examination disclosed a turbid specimen, alkaline in reaction and containing a trace of albumin, and its microscopy revealed profuse mucus and occasional leucocytes, but with no hydatid elements to be seen. It was sterile on culture and estimation of the urinary ketosteroids showed that 4·2 mg. were excreted in 24 hours.

The patient's blood-urea was 14 mg. per cent and the blood-Wassermann reaction was negative. The blood

complement-fixation test for hydatid disease was negative. The white blood-cells numbered 10,700 per c.mm. with no eosinophilia noted.

FIG. 43.—*Case* 1. A left retrograde pyelogram. The upper and middle calices are elongated and distorted and show dilatation of their extremities. The uretero-pelvic junction is situated opposite the tip of the second lumbar vertebra.

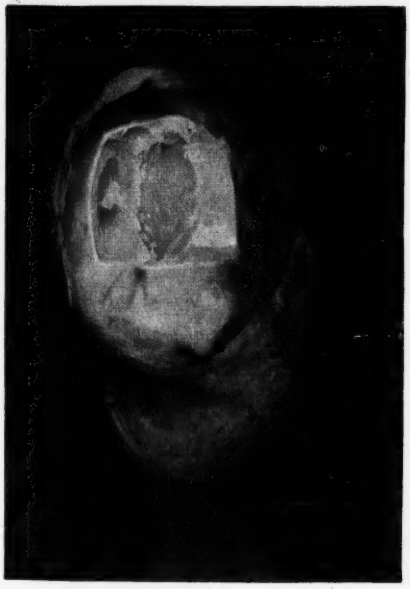

FIG. 44.—*Case* 1. A large hydatid cyst projects from the upper pole and anterior surface of the kidney. Removal of portion of the pericyst and laminated membrane demonstrates the cyst cavity to be filled with daughter cysts and jelly-like debris. A rod has been placed in the ureter and the upper calix of the renal pelvis can be seen stretched out over the top of the cyst. The cyst does not communicate with the renal pelvis.

The Casoni intradermal test for hydatid disease proved to be negative.

A plain radiograph of the patient's abdomen was taken (*Fig.* 41).

An intravenous urogram was obtained (*Fig.* 42).

Left retrograde pyelography was performed (*Fig.* 43).

AT OPERATION.—The left kidney was approached via the lumbar route and a semi-solid tumour was found occupying its upper pole and projecting from the anterior surface of the organ. Its capsule was very adherent to the perinephric tissues. In the course of the subsequent nephrectomy some of the pericyst remained adherent to the peritoneum in the region of the upper pole.

It was only on section of the organ removed that the nature of the condition present was apparent.

THE SPECIMEN.—A photograph is shown in *Fig.* 44.

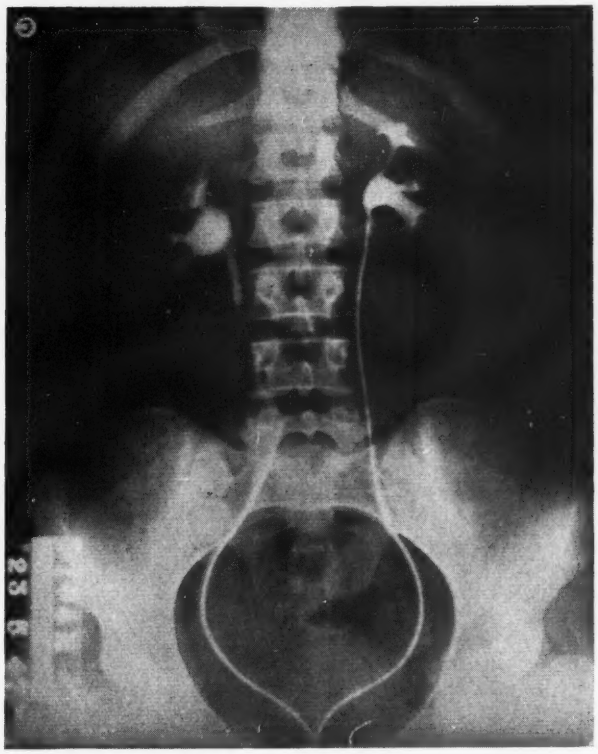

FIG. 45.—*Case* 2. A bilateral retrograde pyelogram. The outline of both renal pelves is normal but the right renal pelvis has been somewhat overdistended with the opaque medium. The right ureter is displaced toward the midline by a large soft-tissue shadow.

Case 2.—A female, aged 33 years, complained of three severe attacks of pain in her right upper abdomen. She had also noticed a swelling in her right loin.

The patient had lived all her life in country districts of New South Wales and had no previous illnesses or operations.

ON EXAMINATION.—The patient was a thin but healthy woman and abdominal examination disclosed that an obvious swelling was present in her right flank. On palpation the right kidney was enlarged, rounded, tender, and movable.

Retrograde pyelography was performed (*Fig.* 45).

AT OPERATION.—The right kidney was approached through a lumbar incision and on exposure its lower pole was seen to be occupied by a large cystic swelling the size of a fœtal head.

The appearance of the cyst wall was so strongly suggestive of a simple cyst that partial nephrectomy was contemplated, but the capsule of the cyst being incised

prior to its projected excision, laminated membrane presented. Right nephrectomy was performed.

THE SPECIMEN.—See *Fig.* 46.

FIG. 46.—*Case* 2. A large univesicular hydatid cyst occupies the lower pole of the right kidney. A window has been cut in the pericyst and the collapsed laminated membrane can be seen in its interior. The cyst has not encroached upon the renal pelvis. Before its puncture, the cyst was the size of a fœtal head.

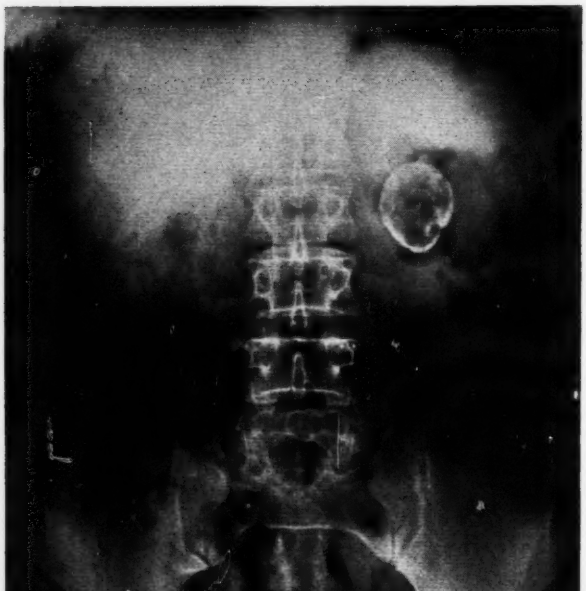

FIG. 47.—*Case* 3. A plain radiograph of the abdomen. There is a large, rounded, calcified shadow lying opposite the tip of the left transverse process of the second lumbar vertebra.

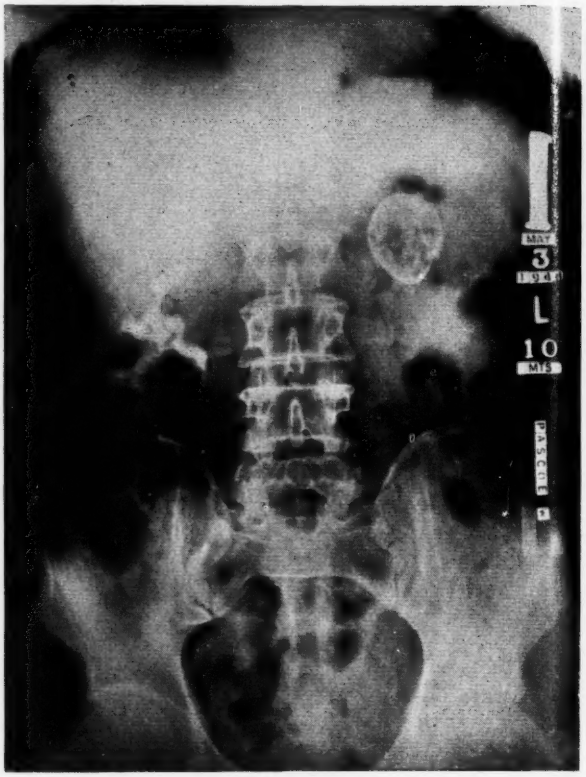

FIG. 48.—*Case* 3. An intravenous urogram. The right kidney shows good function but there is no excretion evident on the left side. The rounded, calcified shadow is apparent as in the plain radiograph.

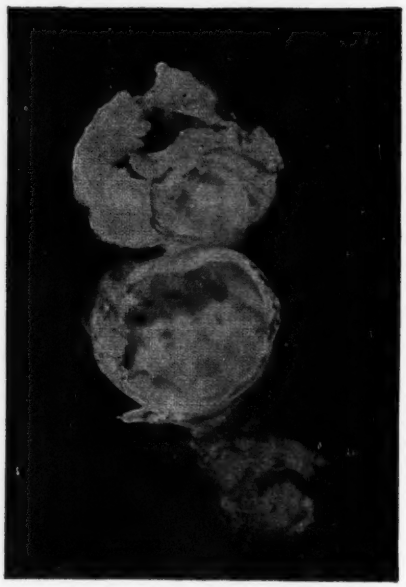

FIG. 49.—*Case* 3. The kidney substance is seen to be replaced by a calcified cyst which has completely replaced the renal parenchyma. Remnants of laminated membrane were detected on microscopy (Prof. H. R. Dew). Apparently this cyst had at some time communicated with the ureter and had completely discharged its contents, followed by death of the cyst. Degeneration and calcification of the pericyst followed, accompanied by obliteration of the ureter. This is an example of spontaneous cure of renal hydatid disease.

Case 3.—A male, aged 61 years, complained of stabbing pains in the left lumbar region of seven months' duration. The pains lasted three to four days at a time, with remissions of a week or less, and were worse after food.

He had lived in Broken Hill 1889–98, 1907, Bendigo 1898, 1915, 1917, 1922, England, Canada, U.S.A., N.Z. (Waihi—a mining town) 1908–10, 1914, 1919–22, and a niece who had lived in Waihi all her life had a "hydatid in the leg". He had suffered from a gastric ulceration in 1940 and 1948, and had frequency of micturition for years. Cystoscopy at an earlier examination had revealed early enlargement of the sub-cervical lobe of the prostate gland.

ON EXAMINATION.—Clinical examination of the patient's heart and chest revealed no abnormality and on abdominal examination no tumours or tenderness were noted.

A plain radiograph of the patient's abdomen was taken (*Fig.* 47).

An intravenous urogram was obtained (*Fig.* 48).

A cystoscopic examination was carried out and the bladder was found to be normal, but a ureteric catheter could not be made to enter the left ureteric orifice and a left retrograde pyelogram could not be obtained.

AT OPERATION.—The left kidney was approached by the lumbar route and its position was found to be occupied by a stony hard, rounded swelling attached to the great vessels by a long, attenuated pedicle. The kidney substance was completely atrophic. The calcified object was removed together with fibrous remnants of the kidney and suprarenal gland.

THE SPECIMEN.—*See Fig.* 49.

Case 4.—In September, 1913, a female, aged 19 years, reported to the hospital complaining of a discharging sinus in her right groin which had been present and had resisted treatment for the previous eight months. There was no family history of tuberculosis elicited and clinical examination of the patient did not disclose any evidence of pulmonary tuberculosis.

The sinus orifice was situated in the upper part of the right femoral triangle just below Poupart's ligament; a malleable probe was passed into the sinus and it was found to extend 8 in. up to the vicinity of the transverse processes of the lumbar vertebræ. A radiograph of the patient's abdomen was taken, the report of which reads as follows: "The sinus appears to lead to the region of the last dorsal and the first lumbar vertebræ. No definite lesion of the vertebræ detected."

Following curettage of the sinus track and filling the sinus with iodoform emulsion, the lips of the sinus orifice were excised and the wound closed. Following this procedure the wound broke down and discharged purulent material and on one occasion it is recorded that "small hard calculi" came from the wound. There is no record of any bacteriological or histological examination of the material curetted from the sinus having been made.

After five months' hospitalization the patient was discharged unrelieved, and the diagnosis of tuberculosis of the spine and right psoas abscess was recorded.

In 1946, at the age of 53, the patient was again admitted to hospital complaining of constant pain in the right loin of seven years' duration. For the past six months attacks of right-sided colic had also been present, during which attacks the pain radiated from the right loin to groin, down the back of the right leg, and into the right knee. There had been no hæmaturia or passage of urinary calculi, but diurnal frequency of micturition had been noticed by the patient. She had noticed a loss of 1 st. in weight over a period of six months.

Since her previous admission to hospital in 1913 she had had six children.

Appendicectomy had been performed sixteen years ago, following which a sinus developed in the wound and discharged for four months.

ON EXAMINATION.—Clinical examination disclosed an apparently healthy woman. There were no abnormal findings discovered on examination of the patient's chest and heart. Abdominal examination disclosed a well-healed but depressed and adherent McBurney incision and a cicatrix at the base of the right femoral triangle, with no involvement of the femoral vessels and with no hernia present. There were no abdominal viscera enlarged to palpation, but tenderness was elicited on palpation of the right hypochondrium.

Investigations.—Blood-urea 54 mg. per cent. Hæmoglobin value 13 g. per cent. White blood-cells 10,200 per c.mm. Neutrophils 57 per cent, lymphocytes 32 per cent, monocytes 7 per cent, eosinophils 4 per cent. *Bladder urine*: Pus formed 80 per cent of the high dry field and

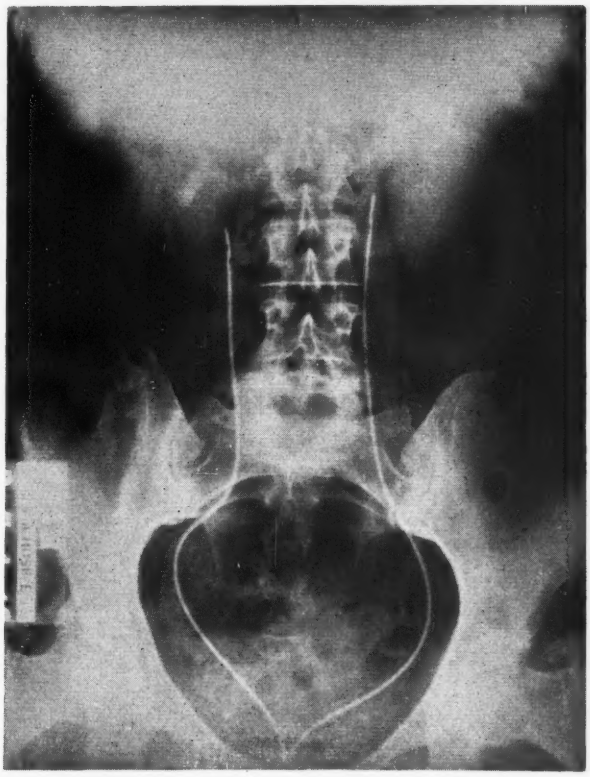

FIG. 50.—*Case* 4. A right retrograde pyelogram. The right renal pelvis is incompletely filled, the opaque medium outlining the middle and lower calices only. The upper portion of the renal pelvis is filled with radio-translucent material.

1–2 red blood-cells per high dry field were seen. The culture of the urine was overgrown by *Bacillus proteus*. *Cystoscopic examination*: No vesical abnormality was noted, but thick pus was seen to exude from the right ureter, the efflux from the left ureter being clear. The right and left ureters were catheterized without any obstruction, and clear urine, which was subsequently found to be sterile on culture, was obtained from the left catheter but no urine could be obtained from the catheter in the right ureter.

A right retrograde pyelogram was taken (*Fig.* 50).

A clinical diagnosis of right-sided pyelonephritis with suppuration was made.

AT OPERATION.—Right nephrectomy was performed through the usual loin incision. There was no perinephritis present and the organ was delivered with ease. The renal pelvis was noted to be full of inspissated material on palpation and the operative diagnosis of the pathological condition present was polycystic disease of

the kidney with suppuration. The true condition present was revealed only on section of the kidney.

THE SPECIMEN.—*See Figs.* 51, 52.

FIG. 51.—*Case* 4. The surface of the kidney is elevated by discrete cystic protrusions, the largest of which springs from the upper pole and measures 5 cm. in diameter; the remainder of the surface of the kidney shows scattered cysts which vary in size from that of a pin-head to that of a cherry.

Case 5.—Five weeks before being seen, a youth aged 14, while at school, had noticed a pain which he referred to his left hypochondrium. This pain had persisted and had become worse during the past few weeks. He did not complain of any urinary symptoms.

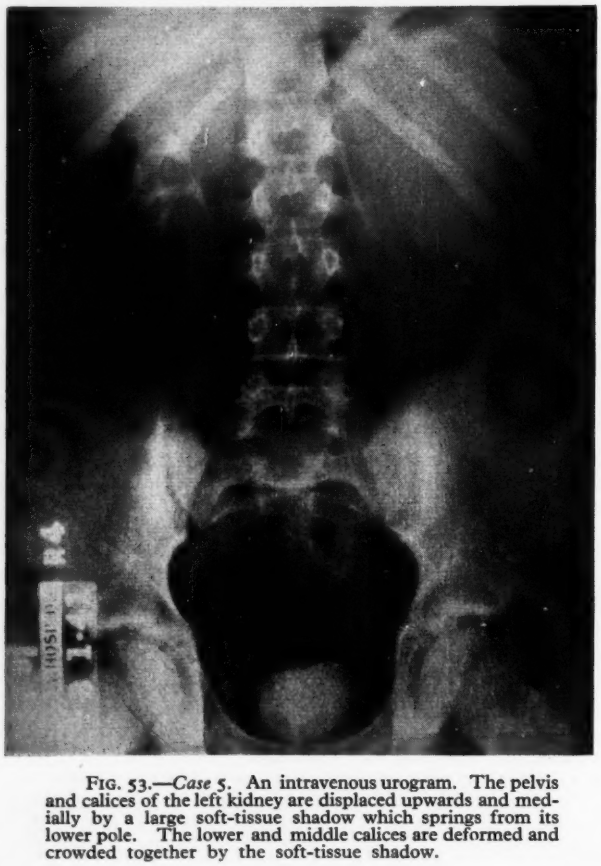

FIG. 53.—*Case* 5. An intravenous urogram. The pelvis and calices of the left kidney are displaced upwards and medially by a large soft-tissue shadow which springs from its lower pole. The lower and middle calices are deformed and crowded together by the soft-tissue shadow.

He was an apparently healthy young boy who had been born in Lithgow (about 100 miles west of Sydney) and had lived in this country district all his life.

FIG. 52.—Same case. A coronal section of the kidney shows that its substance is honeycombed by a hydatid cyst which approaches the surface at many points, but mainly in the vicinity of the upper pole. The cyst has ruptured into the renal pelvis. The laminated membrane has collapsed away from the pericyst and can be seen in the process of evacuation, filling the renal pelvis and passing down the ureter.

ON EXAMINATION.—Abdominal examination disclosed a large swelling with the clinical characteristics of a renal tumour occupying the left hypochondrium and extending as low down as the umbilicus.

Examination of the patient's urine disclosed no abnormality and the hæmatological findings in his case were as follows: R.B.C. 3,900,000; HB 10·3 g. per cent, 71 per cent normal; W.B.C. 6100—neutrophils 59 per cent, lymphocytes 21 per cent, monocytes 10 per cent, eosinophils 8 per cent, basophils 2 per cent. The patient's blood-urea was 30 mg. per cent.

FIG. 54.—The section shows the presence of laminated membrane with granular endocyst still attached to its inner surface. There are numerous brood capsules with scolices present. (H. and E.) (× 400.)

An intravenous urogram was obtained (*Fig.* 53).

A provisional diagnosis of a Wilms' tumour was made and a course of deep X-ray therapy was prescribed as a pre-operative measure.

Four weeks later, on his readmission to hospital, the tumour had become larger.

AT OPERATION.—Left nephrectomy was performed with ease and at the operation the pathological condition present was thought to be a renal neoplasm.

On section of the kidney its lower pole was found to be occupied by a univesicular hydatid cyst measuring 16 × 9·5 cm. Most of the renal tissue had been destroyed by pressure atrophy. The cyst did not communicate with the renal pelvis.

A microscopical section of the cyst wall is shown in *Fig.* 54.

DISCUSSION

Craig and Lee-Brown (1928) state that " on pyelographic evidence there should be little difficulty in differentiating a hydatid from a solid tumour ; the latter causes more spider-like deformity than a hydatid of the same size. Pyelography cannot differentiate between a solitary cyst of the kidney and a closed hydatid ". Whilst the latter part of this contention is fully corroborated by *Case* 2 herein reported, the former cannot be substantiated, as the pyelographic findings in *Case* 1 indicate.

Reay (1941) maintains that " rarely does a renal hydatid cyst come under observation without the presence of a palpable tumour in the lumbar region ". He also affirms that " a lower polar cyst usually presents as an abdominal tumour and displaces the kidney upwards ". The cases reported in this paper do not bear out either of these statements and it would be agreed with Craig and Lee-Brown (1928) that in this disease " it is the hydatid which becomes displaced and not the kidney ".

Case 1 bears out the observation of Dew (1927) and Campbell Begg (1936) that the presence of dense adhesions welding the pericyst to surrounding structures renders nephrectomy difficult on occasions. The latter author observed that a hydatid cyst in the substance of the kidney feels solid and in *Case* 1 this fact prompted the diagnosis of a renal neoplasm at operation.

Case 4 is of special interest in that it eluded diagnosis for a period of thirty-two years. In view of the fact that a positive bacteriological diagnosis of the tuberculous aetiology of the " psoas abscess " had never been made and in the absence of radiological evidence of tuberculous spinal caries, and in view of this patient's subsequent history, it is considered that an hydatid origin of the " psoas abscess " is possible, the primary hydatid cyst being situated in the substance of the right psoas major muscle. This would possibly account also for the patient's symptoms which resulted in appendicectomy and the sinus which persisted for four months after this operation. The absence of perinephritis discovered at the nephrectomy thirty-two years later, and the inspection of the organ removed at operation, would appear to render a renal origin of the " psoas abscess " highly unlikely.

In the five cases reported, an accurate preoperative diagnosis was not made in any instance although hydatid disease was strongly suspected in *Case* 1, but the failure of the immunity reactions led to this diagnosis being waived in favour of a renal neoplasm, and this was thought to be the condition present prior to the pathological examination of the specimen removed. *Cases* 2, 4, and 5, illustrate clearly that prior to complete pathological examination of specimens removed at operation, renal hydatid disease can quite easily be mistaken for simple cystic disease of the kidney, polycystic disease of the kidney, and renal neoplasms.

In *Case* 5 the age of the patient, his clinical condition, the findings on pyelography, and an eosinophilia of 8 per cent were all features strongly in favour of a diagnosis of hydatid disease of the kidney, but this diagnosis was not considered and the pre-operative diagnosis and that at operation was Wilms' tumour of the kidney.

If the organ can be delivered on to the loin, nephrectomy is the treatment of choice for hydatid cysts of the kidney.

SUMMARY

1. Five examples of hydatid disease of the kidney are reported.

2. The interpretation of the pyelogram in cases of ' closed ' renal hydatid cyst can be very difficult and in some cases diagnosis is impossible. A renal neoplasm may present an identical radiological picture and in *Case* 1 this was the diagnosis even at operation.

3. Large hydatid cysts may be present in the polar regions of the kidney and the kidney remain in its normal position. (*Cases* 1, 2, and 4.)

4. A large hydatid cyst of the kidney may be present without a tumour being palpable in the loin. (*Cases* 1 and 4.)

5. Uncomplicated renal hydatid disease is compatible with apparent good health. (*Cases* 1, 2, and 5.)

6. A lateral radiograph of the renal area is the only means of localizing a calcified shadow in the hypochondrium when the ureter is obliterated and the kidney functionless. (*Case* 3.)

7. Renal hydatid disease may cause calcified shadows which occupy the renal area and require differentiation from renal lithiasis and renal calcification of other aetiology. (*Cases* 1 and 3.)

8. At operation hydatid disease of the kidney may be confused with polycystic disease of the kidney, simple cystic disease of the kidney, and renal neoplasms.

9. Under favourable conditions spontaneous cure of renal hydatid disease may occur following rupture of a cyst into the renal pelvis. (*Case* 3.)

I am indebted to Mr. J. W. S. Laidley, Mr. M. S. S. Earlam, and Mr. A. L. Carrodus, of the Department of Urology, Royal Prince Alfred Hospital, Sydney, for permission to publish these case reports. Professor H. R. Dew, Dean of the Faculty of Medicine of the University of Sydney, kindly assisted in the identification of the pathological nature of the specimen in *Case* 3. My thanks are due to Professor Gordon Bell and N. Waddle for the statistical information contained in the Louis Barnett Registry. For the photographic illustration of this article, I am indebted to the Department of Medical Artistry, the University of Sydney.

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AORTIC EMBOLECTOMY

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FROM THE DEPARTMENT OF SURGERY, POSTGRADUATE MEDICAL SCHOOL OF LONDON

ALTHOUGH it seems not unlikely that in these days a good many cases of aortic embolectomy pass unrecorded in the literature, the tally of successful operations is still small enough to warrant an account of two patients treated in our surgical wards within a period of rather less than a year, if only because in these two cases the operation proved much simpler than was expected. It is proper, however, to point out that although in our two cases there was, happily, no immediate loss of life or of limb, the operation in neither case restored the circulation completely to normal.

CASE REPORTS

Case 1.—Mrs. J. C., aged 50. This patient first came under treatment in 1946 with rheumatic mitral disease complicated by paroxysmal auricular fibrillation. Normal rhythm returned spontaneously after a short period of rest in bed, and a presystolic and a diastolic murmur became evident at the apex. There was at the time of this admission no clinical evidence of failure. She was able, after her discharge, to resume housekeeping and to work part-time in a factory.

On Oct. 17, 1947, she complained of feeling cold and out of sorts. This was followed by pain in the right side of the chest and next day by palpitations. There was no hæmoptysis. On her admission to the medical department under the care of Dr. Russell Fraser on Oct. 24, she was found to be dyspnœic and cyanosed and her jugular venous pressure was 4 cm. above the sternal angle. There was slight œdema with pitting over the sacrum, but the liver was not enlarged. The apex beat was felt 4 in. from the midline in the 6th left interspace, and there was a presystolic thrill and murmur. The heart-rate at the apex was about 140 and irregular. There were the physical signs of an effusion at the right base, but no fluid was found on needling. She responded well to intravenous strophanthus and oral digitalis, the ventricular rate at the apex on Oct. 27 being 70, and the jugular venous pressure nil.

On Nov. 4, at 1.30 p.m. precisely, she suddenly noticed that both legs had gone numb, the right as far as the upper part of the thigh, and the left as far as the knee. At the same time she had the desire to pass a stool and called for a bed-pan. Later she was incontinent of fæces and partially, too, of urine, which did not, however, contain any macroscopic blood.

There was at this stage no pain in her legs but she felt hot and was found to be pale and sweating. Twenty minutes after the onset of these symptoms all pulses were absent in each leg but the aortic thrust could be felt just below the umbilicus. The skin was cold to the level of T.10 or T.11 in front and behind. There was tenderness on deep palpation in the hypogastrium. There was some impairment of sensation in the distal part of each limb, and the ankle and plantar reflexes could not be elicited on either side.

A diagnosis of embolism at the aortic bifurcation was made and the patient was brought to the theatre three hours after the onset of her symptoms.

AT OPERATION (Professor Aird).—Spinal anæsthesia (nupercaine 1·6 ml.) giving anæsthesia to the level of the 6th thoracic segment.

With the patient in the Trendelenburg position, the abdomen was opened through a right lower paramedian incision, the intestines being packed off in the upper abdomen to expose the termination of the abdominal aorta and the commencement of the common iliac on each side. The vessels were laid bare by incising the investing layer of peritoneum in the midline and dissecting the two margins laterally.

There was no pulsation in either iliac vessel or in the last 2–3 cm. of the aorta. Aortic pulsation was palpable, however, above this level. One tape was passed around the aorta just at the lowest level where pulsation could be felt, and one immediately above the iliac bifurcation on each side. An incision was now made through all the coats of the left common iliac. No clot was, however, extruded until the vessel on the right side had been 'milked' upwards towards the bifurcation. By further manipulation more firm clot was coaxed out of the aorta, seven fragments in all being obtained (*Fig.* 55). Delivery of the last one was followed

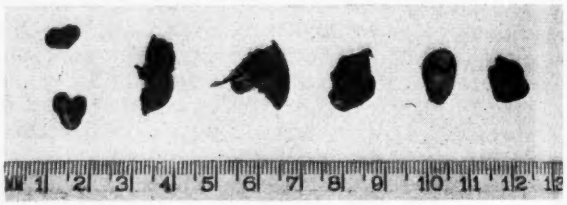


FIG. 55.—*Case* 1. Fragments of clot removed at operation from the aorta.

by a spurt of blood. The upper aortic tape was now rendered taught and each iliac one loosened in turn. There was in each case an immediate return through collaterals from the distal part of the iliac trunk. The opening in the left common iliac artery was now closed by arterial suture stripping back the adventitia and taking pains not to have any of the stitches penetrating the intima. When the suture had been completed, however, it was discovered that the lumen of the vessel had been so much narrowed at the point of repair as to seem unlikely to function adequately and also to be a potential point of origin for post-operative thrombosis. Accordingly, having taken care to see that the vessel on the other side was, in fact, quite patent, a formal arteriectomy of the segment of vessel at the site of exploration was carried out with ligature of the two cut ends with silk.

The operation time was approximately 2¾ hours. Heparin was not administered and it was not considered necessary to give a blood transfusion.

At the completion of the operation the pulses in the right leg were normal and the leg was warm and pink. The left leg pulses could not be felt and the foot on this side was distinctly cold.

Post-operative treatment was by penicillin, digitalis, and distant heating to the trunk and arms. Recovery of sensation and of muscle power was complete by Nov. 6, and on Nov. 7 the temperature of the skin on each foot was approximately the same, although it was still not possible to feel a pulse at any level in the left leg. The results of a reflex heating test are shown in the accompanying graph (*Fig.* 56).

Section of the segment of excised vessel showed the presence of only a little calcification. Blood-clot, too, was present, but it was not possible to give a firm opinion as to whether it dated from the time of operation or from slightly earlier.

PROGRESS.—She was last seen in March, 1949, and up till that time there had been nothing to suggest the

occurrence of any further embolic accidents. She was looking after her home and her husband and was perfectly able to contend with the flight of 37 steps leading to her flat, although she admitted that she had to take it rather leisurely and was somewhat breathless when she got near the top. She could even manage to run a few yards to catch a bus.

The left leg was, however, still somewhat weaker than the right and walking for ten minutes or so led to a troublesome aching in the muscles of the thigh on that side. She had also noticed some tingling and numbness on the dorsum of the left foot and cramping discomfort in the upper part of that leg sufficient to disturb her sleep. Her general condition had remained excellent.

but she did not come for treatment again until March 23, 1948, when she was admitted under the care of Dr. W. Brigden.

At the age of 19 she had developed " heart trouble " following a bout of rheumatic fever, and spent six months in bed. She had suffered ever since from dyspnœa on mild exertion, although she was still able to negotiate one flight of stairs comfortably and slept with a single pillow.

In December, 1947, her left foot suddenly became cold, numb, and painful. She was forced to take to bed, but rose repeatedly to warm the foot in front of the fire. The leg was painful and somewhat swollen during the next few weeks and then seemed to improve. As

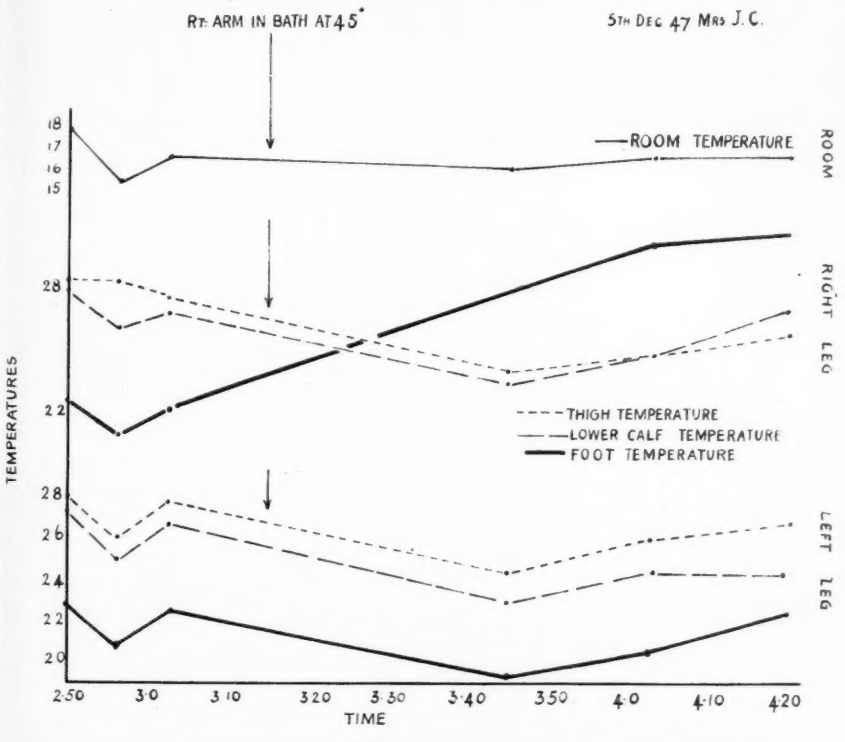


FIG. 56.—*Case* 1. Graph to show result of a reflex heating test one month after operation at which the left common iliac artery was divided between ligatures.

FIG. 57.—Same case. Photograph showing the incision and the condition of the lower limbs sixteen months after operation.

Her resting pulse-rate was 80 and her B.P. 150/90. There was no dropsy and no sign of raised jugular venous pressure. The colour of the two limbs was a healthy pink but the skin of the left foot was perceptibly colder to the touch. No pulses could be felt in the left leg, but they were all present in the right, and there was not the slightest evidence of a precarious circulation in the skin of either limb. There was a suggestion of wasting of the left leg (*Fig.* 57); measurements were as follows :—

Girth	*Right*	*Left*
Mid-thigh	50 cm.	48 cm.
Mid-calf	35 cm.	34 cm.

The muscle power of the left leg was reduced by about 20 per cent, but the only disturbance of sensory function was an area of paræsthesia on the dorsum of the foot.

Case 2.—Miss F. C., aged 40, first came under observation in 1941, at the age of 34, with chronic mastitis. She was found to have rheumatic mitral disease, with dyspnœa on mild effort but without dropsy. X-ray examination showed a prominent conus and an enlarged left auricle and an electrocardiogram suggested mitral and tricuspid stenosis. Hospitalization was advised, soon as she was well enough to move around the house, she found that her activity was considerably restricted by pain in the left calf brought on by the mildest exertion and almost immediately relieved by rest. About a year previously (i.e., in 1946) she had had a somewhat similar but less dramatic episode, the details of which, however, she was unable to recall with any great accuracy. There was, in fact, a considerable degree of mental impairment which made it almost impossible to get a coherent account of her illness. There was at rest no dyspnœa or cyanosis, and only a minimal degree of œdema. The jugular venous pressure was, however, 3 cm. above the sternal angle and her auricle was fibrillating, the rate at the apex being 96. The B.P. was 130/100 and the liver was not palpable.

On the left side the femoral pulse and a rather doubtful popliteal could be felt, but in the right only the dorsalis pedis was absent. A florid countenance matched well a hæmoglobin of 16·3 g. per cent and erythrocyte count of 6,000,000. There was a systolic thrill at the apex and a systolic and diastolic murmur in the mitral area. She was put on digitalis, which had brought the ventricular rate down to 60 by April 8, 1948. That

evening she complained of pain in the right lower abdomen, and vomited. There was tenderness on palpation in this area, but by next morning she had fully recovered and the episode was attributed to over-digitalization.

Late in the evening of April 13 she complained of the sudden onset of numbness in each leg, with pain

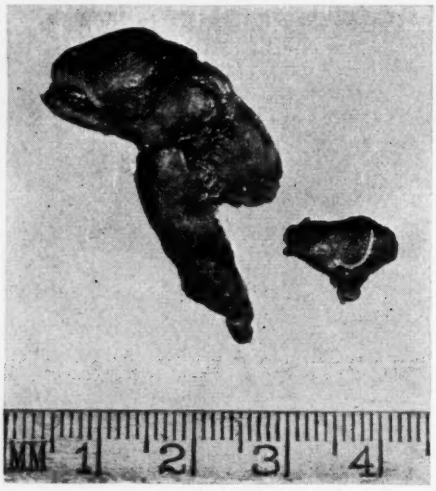


FIG. 58.—*Case* 2. Emboli removed at operation from the aortic bifurcation.

along the line of the left femoral vessels. This was followed by tingling, and despite sedation she spent a disturbed night.

Next morning (April 14) all pulses in each leg were found to be absent and she was still complaining of severe pain in the left thigh and of tingling in the right

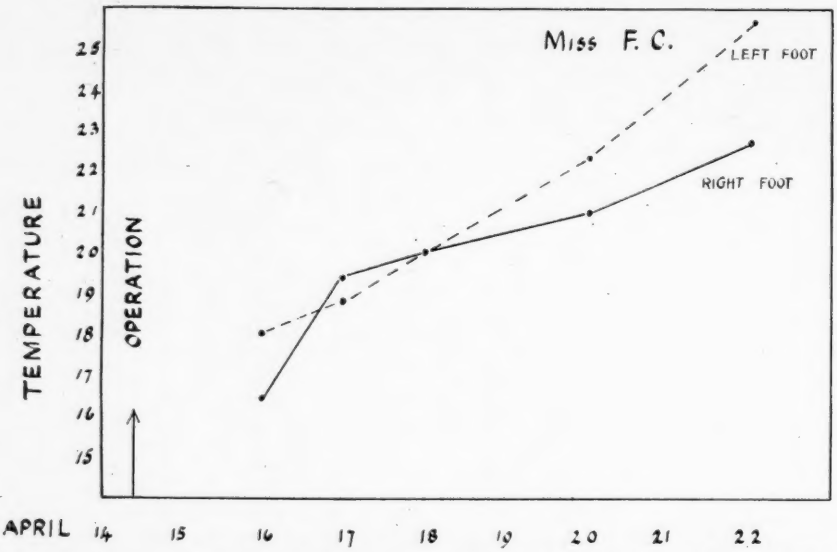


FIG. 59.—Same case. Record of skin temperature of each foot on the days following operation.

foot. The temperature of the skin of the right foot was just over 26° C. and the left a fraction of a degree lower. Neither changed appreciably despite the administration of a variety of vasodilators, viz., amyl nitrite, mecholyl, and tetra-ethyl-ammonium bromide. Sensation was normal but for a small patch of diminished appreciation of light touch on the dorsum of the left foot. There was no loss of sphincter control.

In the early afternoon a confident diagnosis was made of embolism at the aortic bifurcation.

OPERATION (M. R. E.) was begun at 8.15 p.m., almost exactly 24 hours from the estimated time of impaction. A single dose of heparin, 25 mg., was given intravenously during the afternoon, i.e., three or four hours prior to operation, as well as 300 mg. of dicoumarol by mouth. Five ml. protamine sulphate was injected intravenously in the theatre. The abdomen was opened through a midline incision extending from the pubis to about 3 cm. above the umbilicus. The coils of intestine were packed out of the pelvis to display the aortic bifurcation. At first it was thought that there was pulsation in the iliac vessels, but it later became apparent that this was not expansile pulsation but only a transmitted thrust directed along the line of each vessel from the aorta. There was forcible pulsation in the aorta about 2 cm. above the bifurcation, but distal to this point the artery was non-pulsatile and had a solid feeling which suggested that there was a clot inside. The peritoneum was incised to display the bifurcation and the iliac vessels. The net-work of veins and nerves in this area was divided between forceps to give an adequate exposure. The common iliac artery on each side was controlled by a small ' bulldog ' clamp just above its bifurcation. Two red rubber catheters were passed under the aorta about 2 cm. above the bifurcation after the last left lumbar artery had been secured between ligatures. The catheters were tightened and secured by artery forceps. A longitudinal incision about 1 cm. was now made in the right common iliac artery. From this opening there immediately herniated a firm clot. The remainder of this firm clot was ' milked ' out of the aorta and from the commencement of the left common iliac artery. On releasing the distal clamps blood regurgitated satisfactorily, but on releasing the aortic tourniquet no blood flowed. It now became apparent that there was a second small clot and after its removal there was a vigorous discharge of blood from the aorta. The controlling clamps were now reapplied and the incision closed, using interrupted waxed silk, sparing the intima. On releasing the aortic clamp the suture line was found to be by no means watertight, but this was quite satisfactory after two further sutures had been inserted. At this stage, however, it was disappointing to note that there was no pulsation in the vessel distal to the line of suture. The vessel at this level was also noticed to be much narrower than at the corresponding level on the opposite side and the lack of pulsation was considered to be due to spasm rather than to an overlooked embolus, but there was still no pulsation after its adventitia had been infiltrated with 1 per cent procaine. On finally releasing the aortic tourniquet there was a brisk ooze from somewhere behind the aorta, but this was controlled by a few minutes' pressure on gauze. The rent in the peritoneum was closed and the abdominal wall secured in layers. At the conclusion of the operation there was a reasonably good left femoral pulse but none was present on the right side.

The operation took 1 hr. 40 min. The pulse-rate and blood-pressure remained quite unaltered throughout.

PATHOLOGY REPORT ON EMBOLUS FROM AORTIC BIFURCATION (*Fig.* 58).—" Specimen consists of a clot

1·7 cm. in diameter, with two arms each 0·6 cm. Histologically it is a recent clot without signs of organization."

PROGRESS.—At no time after operation did the general condition give any cause for anxiety, the heart rate being readily controlled by digitalis.

By next morning (April 15) all the pulses could be felt in the left leg, but the right femoral was still absent. On April 16, each leg felt warm down to the mid-calf level.

The circulation in each foot continued to improve, the skin temperature readings rising, as shown in the accompanying chart (*Fig.* 59).

By April 18, however, she had developed a huge decubitus ulcer over the sacrum, which healed very slowly.

By May 8 she was able to walk quietly about the ward, but the epithelium over both heels and from small areas on several toes had shed to leave shallow ulcers (*Fig.* 60).

She was finally discharged home by ambulance on June 16.

The following entry was made in her case record when she was visited in her own home in March, 1949 :—

"Since her discharge from hospital she has been confined to the house. Three or four months elapsed before her sacral sore was firmly healed. She still spends the morning in bed, but is able without assistance to move from room to room. She sleeps comfortably with only two pillows and there is no dropsy and no liver enlargement. The heart-rate is adequately controlled by digitalis. Her only complaint is that she has great difficulty in keeping her legs warm when she is up and about. There is no history to suggest that she has had any further embolic episode. Exposure of the left leg to cold brings on a constant aching discomfort.

FIG. 60.—Same case. To show the condition of the feet two weeks after operation.

"Each leg below the knee is somewhat pale, and the skin of the foot is distinctly colder than that of the forearm or hand (although tested immediately after folding back the bedclothes). No pulse can be felt in the groin on either side, or anywhere below this level. Even when deep pressure is made through the widely separated recti in the subumbilical incision, no aortic pulse can be felt. The radial pulse, too, is not easy to detect at either wrist.

"There is no sign of gross circulatory insufficiency in either foot. The pressure sores on her left heel and over the sacrum are both firmly healed and the skin, apart from its pallor and coldness, is of normal texture. Motor power is unaffected and there is no sensory impairment."

Rather less than a month later she had, however, a further and this time fatal embolic accident. At 4.0 p.m. on April 7, she suddenly collapsed. Her mother said that she was then pale and limp and seemed for a short time to lose consciousness completely. Later she was able to mumble incoherently and complained of acute abdominal pain. This persisted without remission during the next 2 hours when she passed per rectum a large quantity of bright red blood. At 8.0 p.m. she first complained of pain in the lumbodorsal region.

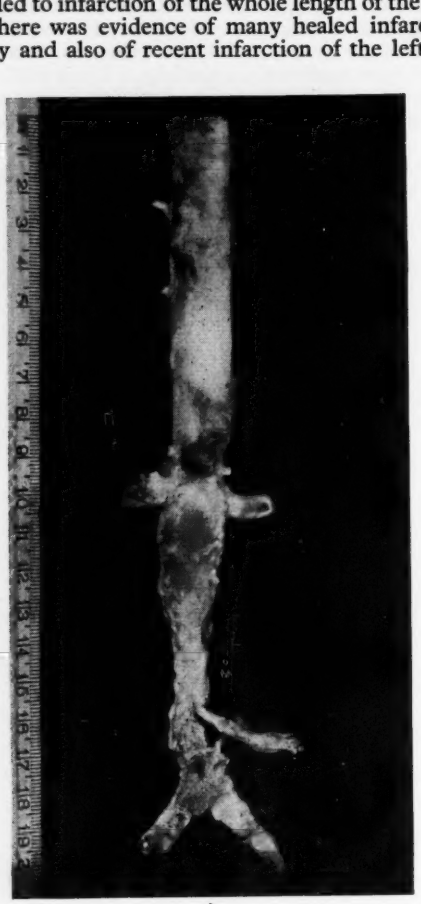
FIG. 61.—Same case. The posterior half of the opened aorta, showing the recent clot in the renal vessels, the rather older clot below this level, and the complete disappearance of the lumen at the bifurcation.

She was admitted to hospital as an emergency about 24 hours after the onset of this acute episode. She was then pale, cyanosed, and pulseless, the ventricular rate being 160 per min. or thereabouts. The abdomen was distended and tender, but not rigid, and there were no bowel sounds. A few crepitations could be heard at each base. At 7.0 p.m. she complained of pain in the left leg, which was noticeably colder than the right. On catheterization the bladder was found to be empty, although no urine had been passed since the beginning of the attack 27 hours before. It was presumed that the aorta was occluded by clot which had now extended to include not only the inferior mesenteric artery, but in view of the anuria and backache, probably the renal arteries as well.

She was given a blood transfusion and heparin 5000 units intravenously 3-hourly. She rapidly went downhill, however, and died at 9.0 a.m. on April 9.

AUTOPSY FINDINGS.—The heart was dilated and the myocardium flabby. There was a thrombus in the left auricle. The mitral valve was represented by a small fibrotic ring which barely admitted the tip of the little

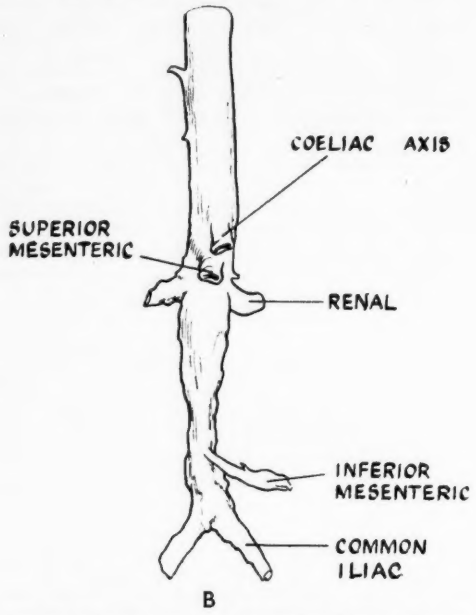
finger. An embolus impacted in the superior mesenteric artery had led to infarction of the whole length of the small bowel. There was evidence of many healed infarcts in each kidney and also of recent infarction of the left one.



A

the bifurcation. Below this level it was very considerably reduced in girth, its wall at the same time being tremendously thickened. The lumen of this segment of the vessel was, in fact, largely obliterated (except in its upper 1–2 cm.) by the firm connective tissue of an old and completely organized clot which had also long since occluded not only the commencement of each common iliac vessel but the inferior mesenteric as well (*Fig.* 62). From section of the clot at three levels, our pathologist (Dr. Evans Pearse) was of the opinion that :—

1. The thrombus in the renal vessels was no more than 2–3 days old (*Fig.* 63).



B

FIG. 62.—Same case. A, Autopsy specimen of aorta, showing its main branches. B, Key to photograph.

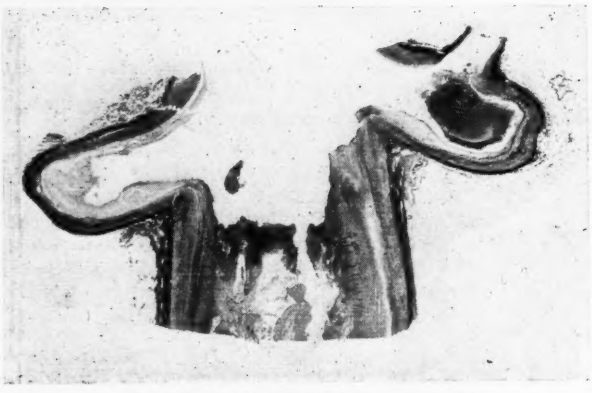


FIG. 63.—Same case. A longitudinal section of the aorta at the level of the renal arteries.

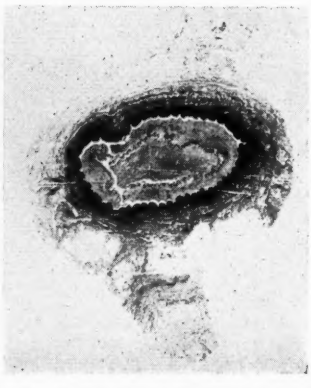


FIG. 64.—Same case. Transverse section of the common iliac artery.

Thanks to the courtesy of the coroner's pathologist we were able to obtain the abdominal aorta and the common iliac vessels (*Fig.* 61). The proximal part of the abdominal aorta was of normal calibre and thickness. The lumen of the cœliac axis was clear, but the origin of the superior mesenteric trunk was closed by a firmly impacted recent embolus. The lumen of the aorta distal to this point was almost entirely occupied by clot. There was extension of this thrombus into each renal vessel, but occlusion on the right side did not seem to be complete. The aorta was of normal dimensions as far as a point roughly midway between the renal vessels and

2. The clot in the distal part of the aorta, including that in the inferior mesenteric and in the common iliac (*Fig.* 64), since it had become almost completely cleared of pigment, was probably over six months old.

3. The thrombus below the level of the renals was between a few weeks and two months old (*Fig.* 65).

DISCUSSION

McClure and Harkins (1943) reviewed the recorded cases of successful aortic embolectomy and were able to add one other to the total of 19

which they had been able to trace in the literature up to that time.

In our more recent search of the literature from 1943 to the beginning of 1949 we have been able to find only 4 more cases, and these all in the journals of the English-speaking countries.*

FIG. 65.—Same case. A longitudinal section taken to include the point where the aorta became much reduced in girth.

Agar (1943) had his case, a young man of 28 with mitral stenosis and fibrillation, on the table within two hours of the impaction of the clot. A transperitoneal approach was employed, using spinal anæsthesia, and no difficulty was found in dealing with the intestine. The technique he employed was direct and simple. The aorta and common iliac vessels were controlled by rubber slings, but the distal ones were only tightened when the head of clot and its trailing ' tail ' of secondary thrombus had been removed. It was extracted through a vertical median incision above the aortic bifurcation. No heparin was then available, but the circulation was fully restored two hours after operation and remained so during the next five months, when he was lost to view.

In 1945 Linton added another, this time, as is typical, a young woman (aged 39) with rheumatic mitral disease and fibrillation. Operation was performed within three hours and heparin was given for twenty-four hours in the immediate post-operative period. The circulation remained excellent in each foot sixteen months later. He, too, advocated the transabdominal approach and emphasized the necessity not only of early but of gentle manipulation and of meticulous suture to prevent consecutive thrombosis. He described a variant of the Nelson lobectomy clamp which was devised to give perfect control of hæmorrhage when the common iliac vessel is incised, and which he claimed is in no way damaging to the intima at the site of occlusion.

J. L. Keeley (1948), operating at six hours in a woman of 52, employed general anæsthesia and a transperitoneal approach. The incision was in this instance made at the junction of the aorta and the right common iliac, and no heparin was used. The only persisting local disability was some dependent œdema of the left leg and some weakness, too, of the peroneal muscle group on that side.

The embolus in Holden's case (1948) came from the roughened endocardium at the site of an old coronary infarction. Admitted to hospital within an hour, spinal anæsthesia was induced forthwith but without relief. Through a transperitoneal approach, and under spinal anæsthesia, each common iliac vessel was then explored, following which there was a complete return of distal pulses in each extremity. He died on the twelfth post-operative day from a new coronary infarction. Heparin was given post-operatively and at autopsy the suture lines in each vessel were healed and free from any sign of clotting.

Nothing can profitably be learned by a further detailed review of the clinical picture of saddle embolism. It has already been done most adequately by several authors, notably by Rothstein (1935), McClure (1943), and others. However, in the consideration of our own two cases, along with the four recent ones which we have abstracted above, there are several points perhaps worthy of consideration.

1. Diagnosis.—The importance of early diagnosis is generally accepted, but its accomplishment is not the easy matter which the classical clinical description of this emergency would suggest. Our first case, besides presenting conveniently, not only in hospital but in the comfortable hours of the middle of the day, was so dramatic and clear-cut as to leave the diagnosis from the very outset in no reasonable doubt. In the second, however, a previous episode of right lower abdominal pain, five days before, had suggested the likely diagnosis of subacute appendicitis. The events during the twenty-four hours which elapsed between the presumed time of impaction of the embolus and operation were in no sense dramatic, and the diagnosis was based alone on close observation of the physical signs. The importance of recognizing this more quiet and insidious presentation has, it is true, been pointed out before by Hermann, Willis, McKinley, and Karotkin (1943), not only as it occurs in saddle embolism but also in impactions farther towards the periphery.

2. Approach.—It will be noted that in each of these 4 cases we have cited, the approach was, as in those which we now present, transperitoneal.

Murray (1943), who published what must be the largest personal series (5 in number), used in every instance an extraperitoneal approach and encountered in the doing of it no great difficulty. However, the transperitoneal has, we believe, the advantage of simplicity and is more likely to appeal to the general surgeon who is so commonly called on to explore the lower part of the abdominal cavity for other causes. Using, as is the common practice, spinal anæsthesia along with the Trendelenburg position, the collapsed intestine can readily be packed out of

* H. L. Allbright and F. C. Leonard (*New Eng. J. Med.*, 1948, **242**, 271) had traced 26 successful cases up to September, 1949.

the pelvis to give a most adequate view of the aortic bifurcation. It is reasonable, however, to suppose that in a case where an exploration of the lower abdomen had previously been undertaken, the extraperitoneal exposure would offer an easy alternative to what might be a tedious and time-consuming intraperitoneal dissection.

3. Anæsthesia.—In correspondence which followed Agar's report (1943) Daley noted that in the previous year, in St. Thomas's Hospital, he had seen 2 cases where the diagnosis of saddle embolus had been made. At operation the embolus was found in each case to be in fact more peripherally situated and this he sought to explain by the distal migration of a clot following the arterial relaxation which accompanies spinal anæsthesia. He used this as an argument for giving the spinal in the ward and waiting an hour or so before making the final estimate of the site of lodgement of the embolus. It was no doubt such considerations which prompted Holden (1948) to try in his case the initial effect of spinal anæsthesia before going ahead with operation. Whether or not it is desirable to await and to encourage distal migration of the clot is a matter which we shall discuss below.

4. Pulsation.—The distal thrust along the line of the common iliacs, even when they are completely occluded by clot straddling the bifurcation, may be disconcertingly like the true pulsation from contained blood under changing pressure. This is so even when the vessels are clearly exposed at operation, and more convincing than the absence of a truly expansile pulse is the unmistakable feeling of a rubbery clot in the lumen as the vessel is palpated between finger and thumb. This point has already been noted by Nordentoft (1929).

5. Control of Hæmorrhage.—Adequate control of the circulation is as essential here as in any operation which involves the opening of large vessels, and it is only when this is complete that a safe and unhurried exploration can be accomplished. There is no doubt that clamps such as Linton (1945) describes are not only mechanically more adequate and in their action less destructive than most of the other instruments commonly employed, but in their absence a soft, red rubber catheter or length of tape folded over, held taught and secured by a pair of artery forceps, proved in our hands perfectly adequate. A catheter can readily be pulled back under the aorta with a long pair of artery forceps gently insinuated and taking care to avoid the lumbar vessels and the vena cava.

'Bulldog' clamps, which were used in our second case for distal occlusion of the iliac vessels, are rather too liable to slip, to be used safely in the control of such large vessels. It must be remembered, however, that the experience gained from operation in the young subject, as is common in the case of rheumatic mitral disease, where the vessels are elastic and resilient, is very different from the problem of dealing with the tortuous calcified trunk of the old man with arteriosclerosis who has an embolus from an intimal clot in the aorta or from the roughened endocardium lining a myocardial infarction.

6. Incision in Vessel.—There is, we believe, a strong argument for making the incision, as was done so successfully by Agar (1943), in the aorta itself. Direct access is thus afforded to the embolus as it lies straddling the bifurcation, and it can presumably be withdrawn intact along with its secondary trailing 'tail' in the iliac vessels before the distal clamps are closely applied. There is certainly thereby less risk of the excessive narrowing which may follow closure of an incision in an iliac vessel, which led in both of our cases to a failure of restoration of the blood-flow and in one even to sacrifice of a segment of the vessel itself.

In our second case we made the mistake, too, of choosing for our incision the vessel which appeared to be the least extensively occluded. We should more wisely have made our incision in the more seriously affected trunk and thereby not have compromised the healthier one.

Again it must be admitted that exploration of the aorta itself might be a hazardous business in the older individual.

7. Method of Removal of the Clot.—Any intraluminal manipulation, be it the energetic use of a metal probe or only the gentle searching of suction applied to a lubricated catheter, is probably undesirable (Linton, 1945). Any breach in the intima, however small, increases the risk of subsequent thrombosis, and in any case neither of the above measures is likely to lead to more than an unsatisfactory and incomplete removal of piece-meal clot. We have been impressed by the energetic herniation of the clot under the *vis a tergo* of the pressure in the aorta.

Murray (1943), having delivered the clot without any proximal aortic clamp, speaks of a spurt of blood following its complete removal rising to 6–15 ft. The aortic pressure, aided by gentle 'milking' just behind the clot, is best calculated to lead to total removal of an unbroken clot. The photographs of our operation trophies unfortunately show only too well how far short we fell of the ideal.

Inherent in the indirect method of removal by exploration of the femoral vessel below the groin on each side is the difficulty of knowing when the removal has been complete, and the amount of intimal damage is no doubt directly related to how assiduously the surgeon endeavours to demonstrate an unobstructed vessel on each side. It must be difficult even at the end of such manipulations to decide whether or not the clearance is satisfactory.

8. Ancillary Measures.—It would seem wise to give heparin during the first few days of the post-operative period in all cases, and especially so if the operation had been carried out at a late stage. It would be particularly valuable, too, if the removal of the clot or the subsequent vascular suture had involved any risk of serious damage to the vessel wall.

The giving of heparin in our second case some hours before the exploration no doubt postponed the occurrence of consecutive thrombosis and lessened somewhat the great risk of failure in an operation so long delayed. In fact, heparin might be given with some justification in the interval which must in most cases elapse between diagnosis and operation, in the knowledge that its effect can immediately be reversed by protamine sulphate.

It is difficult to assess the value of other measures such as paravertebral block and papaverine, and we have no comment to make on their use.

9. Effect of Incomplete Restoration of Blood-flow.—In a young subject with healthy resilient vessels occlusion of one common iliac does not necessarily lead to loss of a limb on that side. The anastomosis across the pelvis from the opposite internal iliac is a most adequate one, as is abundantly demonstrated in both of our cases. Occlusion of each, however, as is the case where a saddle embolus effectively blocks each opening, invariably leads to gangrene. Cases of spontaneous cure following non-operative management of aortic embolism are probably cases where the diagnosis has been inaccurate, or where the clot has been broken and disimpacted, with distal migration to a point where unrelieved obstruction has not seriously jeopardized either limb (Neuhof, 1932). The possibility of spontaneous cure, even in these days of heparin and effective vasodilator drugs, is, however, so remote that in our opinion no case other than the near-to-moribund should be denied the chance of operative removal. The operation is, in fact, not a formidable one. There might, however, in a poor-risk subject, be an argument for the simple fragmentation of the clot by extravascular digital manipulation and fragmentation of the clot alone—la thrombotripsie: Funk-Brentano (1938)—as has been successfully practised by Linnell and Piercy (1949) in the management of recurrent emboli at a slightly lower level.

In our second case autopsy revealed a complete occlusion of both common iliac vessels and of the distal half of the aorta which was considered to be about six months old. We had no opportunity of examining in detail the collateral circulation, which was sufficient, it seems, to provide for the muscular effort of gentle ambulation. It is of interest, too, that the functional activity of the colon was in no way affected by a long-standing obliteration of the inferior mesenteric: the more so, when one bears in mind that there was no free access of blood from the internal iliac and through the middle and inferior hæmorrhoidal vessels.

10. Prognosis.—Long survival after this operation, performed during a period of cardiac failure, is not to be expected. Further embolic episodes are almost inevitable and often occur disappointingly soon after a successful operation. Such considerations are, however, no argument for any slackening of one's resolution, since, according to McClure (1943) the longest surviving patient up to 1943 was operated on for a saddle embolus on two occasions within a period of one year. Impaction of an embolus in a cerebral vessel is often the ultimate cause of death.

That a fatal issue may, however, be for some time delayed is shown by our cases, death occurring twelve months after operation in one, and the other still surviving at sixteen months. Even more encouraging is the fact that she is fully active and happily engaged in her home. In general, the results of conservative measures alone are disastrous to life or to limb and more commonly to the former (Reich, 1943).

11. Time of Embolism.—It has always been believed hitherto that the risk of embolism is considerable at the time when there occurs some fundamental change in cardiac rhythm, and especially when a fibrillating auricle changes to normal regular contraction. More important, however, is the assertion that embolism at the aortic bifurcation (and at other sites) is especially liable to take place when the ventricular rate is rapidly reduced by intensive dosage with digitalis or its equivalent (Reynolds and Jirka, 1944). It should be noted that in each of our cases, and also in that reported by Agar, a striking fall in the pulse-rate had been achieved during the ten days immediately prior to embolism. It has indeed been claimed by de Takats, Trump, and Gilbert (1944) that digitalis itself may be in the first instance largely responsible for the formation of the parent clot. Struck by the apparent close association between digitalis dosage and the occurrence of embolism, they found experimentally in animals that digitalis seems to favour thrombus formation and that this effect is not countered by either heparin or dicumarol. This observation may be of some clinical importance: the knowledge that a patient had in the recent past been on heavy digitalis dosage might support a diagnosis of embolism when the history and physical signs were equivocal.

12. Sex.—For some curious reason, for which we have not been able to find any adequate explanation, embolism, which in roughly 50 per cent of cases is due to rheumatic mitral disease with fibrillation (Reich, 1943), occurs predominantly in female subjects. In this respect the cases which we now record are true to type.

SUMMARY

Two cases of successful aortic embolectomy are reported. The first is still surviving at sixteen months, but the second died twelve months after operation from a further embolism.

Our experience certainly suggests that even in the severely affected cardiac cripple with signs of failure, operation may be very much worth while.

We have been able to trace in the literature reports of 23 successful operations for ' saddle ' embolus.

My thanks are due to Professor Aird for his helpful criticism in the preparation of this paper. For the sections I am indebted to the staff of our Department of Pathology, and for the microphotography to Mr. E. V. Willmott, F.R.P.S.

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APPENDICITIS—A REPORT ON ITS SOCIAL PATHOLOGY AND RECENT SURGICAL EXPERIENCE

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I. MORTALITY AND MORBIDITY

In 1939 the Medical Research Council published a report by Young and Russell on appendicitis in which the authors studied the various aspects of the mortality in England and Wales during the period 1911 to 1932 and also investigated morbidity, particularly in some of the large voluntary hospitals in London. They showed that the mortality at ages under 5 and over 45 years had definitely increased during the period under review, whereas at the intervening ages it had rapidly declined. Furthermore, the statistics relating to the frequency of appendicitis not only confirmed that the disease was very prevalent but also indicated that it had apparently increased. For example, among the insured population of Scotland the annual incidence increased appreciably even between 1930 and 1938, but this increase was not accompanied by any upward trend in the general sickness rate. A part of this increase could probably be accounted for by unnecessary appendicectomies, for the operation, as its safety has increased, has been more frequently performed on account of abdominal pain due to causes other than appendicitis. The diagnosis, in the absence of any other explanation of the pain, is commonly allowed to stand.

Although there was this apparent increase in the incidence of the disease, there was adequate evidence to indicate that the case-fatality had fallen considerably—a result probably due to improvements in diagnosis and treatment and the reduction of preoperative delays.

A similar trend to that observed in England and Wales was also evident during the same period in the American mortality statistics. According to recent evidence, however, published by the Metropolitan Insurance Company of New York (1946), there has been a very substantial reduction in the all-ages mortality from appendicitis between 1940 and 1943 in the United States—an average decrease of 37 per cent and, in some individual states, of as much as 63 per cent. The factors alleged to have produced this decrease are: (*a*) Chemotherapy in cases complicated by peritonitis; and (*b*) Educational campaigns which effectively warned the public against delay in seeking medical advice and against the use of purgatives in the presence of abdominal pain.

In view of (1) the American results and their suggested explanation, and (2) the fact that in the Statistical Report of the Health of the Army (1948) appendicitis was listed third in the main causes of sick wastage (days spent away from the unit and in medical establishments) among women in the Auxiliary Territorial Service during the war, it seemed of interest not only to review the recent statistical history of the mortality from the disease in England and Wales, but also to amplify the study by the inclusion of an analysis of data relating to all cases of appendicitis admitted to the Radcliffe Infirmary, Oxford, during the four years, 1945–8. Such is the purpose of the present study.

1. Age Mortality and Its Secular Trend.—In 1946 there were 867 deaths from appendicitis among males and 668 among females in England and Wales. A discussion of the importance of the disease in terms of its total mortality will not, however, be sufficiently instructive because the death-rates at different ages vary in their significance. This will be inferred from an inspection of *Table I*, which contains the mortality-rates in age groups in England and Wales at intervals since 1920. As official alterations had been made in 1940, both in the classification of the causes of death and in the method of selection between jointly stated causes of death, the rates for the first two triennia have been amended on the basis prescribed by the Registrar-General, so as to bring them into alinement, as far as possible, with current practice.

Table I.—The Death-rates from Appendicitis per 1,000,000 of the Population of Males and Females at Age Periods in England and Wales during Several Triennia

Period	Age Groups								
	0–4	5–14	15–24	25–34	35–44	45–54	55–64	65–74	75+
Males:—									
1920–2	44	108	109	64	71	91	112	109	109
1930–2	62	91	85	64	75	108	162	188	185
1940–2	54	67	73	49	47	61	95	123	147
1945–6	44	51	46	23	31	48	73	112	117
Females:—									
1920–2	29	87	64	46	53	64	70	86	69
1930–2	41	64	41	39	46	79	104	130	132
1940–2	27	43	32	24	26	39	55	86	90
1945–6	23	35	20	17	20	31	47	68	85

Descriptively, it may be said that the age mortality has two peaks in its distribution. The death-rate, is, on the whole, lowest at age 0–4 years, and increases appreciable at 5–14, where the first peak occurs—a peak higher for boys than for girls. This is followed by a decline extending over the next twenty years of life, and it is only when age 55 is reached that the mortality exceeds, and continues in excess of, the death-rate among children of school age.

In many ways the secular trend between 1920 and 1946 is satisfactory. The decline in the mortality between ages 5 and 45 years was continuous for females, and nearly so for males, and the increment which Young and Russell noted at the other age periods between 1920 and 1932 was subsequently arrested. The statistics for 1945–6 thus generally indicate that substantial progress has been made in controlling the mortality from appendicitis. But there is still room for further improvement, because the death-rate among boys under 5 years of age was,

at the close of the period under review, still equal to that in the period 1920-2.

2. Sex Ratio.—A comparison of the male and female mortality at each age period (*Table II*) reveals

Table II.—THE SEX RATIO $\left(\frac{F}{M}\right)$ OF THE MORTALITY FROM APPENDICITIS IN ENGLAND AND WALES DURING SEVERAL TRIENNIAL PERIODS
(*Females per* 100 *males*)

PERIOD	AGE GROUPS								
	0–4	5–14	15–24	25–34	35–44	45–54	55–64	65–74	75+
1920–2	66	81	59	72	75	70	62	79	63
1930–2	66	70	48	61	61	70	64	69	72
1940–2	50	64	44	48	55	64	58	70	61
1945–6	52	69	43	74	65	65	64	61	73

a dominant male sex ratio $\left(\frac{F}{M}\right)$. It is observable in each triennium. On the average, the female death-rate is approximately 40 per cent less than that for males—at ages 15–24 years it is more than 50 per cent in defect. Even when allowance is made for the social stratification of the population, the sex disparity in the mortality is evident. A phenomenon like this, although based on mortality, yet so consistent in its appearance, seemingly indicates a higher incidence or occurrence of appendicitis in males than in females. There is no reason to suppose that the disease, once it has occurred, offers greater surgical difficulties or has greater involvement in the male sex. Furthermore, the male admissions with true appendicitis to the Radcliffe Infirmary during the four years 1945–8 exceeded those for females—the numbers being 591 and 483 respectively. The distribution of these cases according to the Grey Turner classification (mentioned later) did not show any sex difference, i.e., the percentage of female patients who had either peritonitis or abscess was almost identical with that for males; they were also alike in their social grading. Hence the total evidence indicates that appendicitis is more frequent among males than females.

3. Regional Mortality.—Owing to the difficulty of ascertaining the age-distribution of the population in the various regions of the country, it was not possible to calculate the death-rate from the disease for each particular area. As a substitute the method of proportionate mortality was used, whereby the deaths from appendicitis are expressed as a percentage of the deaths from all other causes. This method of statement, being the ratio of two variables, has obvious statistical defects, especially as regards the index at all ages, when used for comparative purposes. Its unsuitability is, however, less pronounced when adopted for specific age periods, since Greenwood and Tebb (1919) have shown that, for a series of districts in which the population at risk in each was not less than 50,000, there was for the age group 35-45 years " a substantial correlation between the ratio of the phthisis deaths to deaths from other causes within the age group and the actual mortality-rate from phthisis at that age group ".

Accepting the index as an approximate assessment for comparative purposes, the relevant ratios at different age periods were calculated for England and Wales and its twelve major geographical divisions. The relatively greater concentration of the disease on children of school age was apparent. The proportionate mortality for boys was 4·31 per cent, and it ranged from the minimal value of 3·32 per cent in North I (Northumberland and Durham) to a maximal of 6·87 per cent in Wales II (mainly the mid and northern counties of Wales). For girls the ratio was lower than that for boys, in the country as a whole (3·55 per cent) and in each geographical area. The lowest index (1·85 per cent) was again evident in North I, but the maximum value (4·71 per cent) was found to be in the South-Eastern Counties outside Greater London. For adult life the ratios had no peak value such as was observable in the death-rates (*Table I*). The disappearance is, of course, due to the fact that, at this period of life, other diseases become numerically much more important than appendicitis as a cause of death.

4. Urbanization.—A similar analysis, made for town and country, is shown in *Table III*, and reveals at every age period, except at age 0–4 in urban districts, a progressive increase in the size of the ratio with decreasing density of population. At age 5–14 the incidence of deaths among boys in county boroughs was 3·74 per cent, in rural districts 4·85 per cent. The corresponding values for schoolgirls were 2·48 per cent and 4·47 per cent respectively. This negative correlation between urbanization and mortality is understandable because, in rural districts, we should expect to find (1) a slower acceptance or awareness of the disease, (2) a greater delay in seeking medical advice, (3) a further delay in obtaining admission to hospital, and (4) sometimes, lower standards of surgical skill.

Table III.—THE DEATHS FROM APPENDICITIS EXPRESSED AS A PERCENTAGE OF THE DEATHS FROM ALL OTHER CAUSES DURING THE PERIOD 1940–6 IN COUNTY BOROUGHS AND URBAN AND RURAL DISTRICTS OF ENGLAND AND WALES

	MALES, AGE GROUPS					FEMALES, AGE GROUPS				
	0–4	5–14	15–44	45+	*All Ages*	0–4	5–14	15–44	45+	*All Ages*
County Boroughs:— Percentage	0·24	3·74	0·98	0·23	0·36	0·18	2·48	0·80	0·19	0·29
Urban Districts:— Percentage	0·34	4·74	1·36	0·26	0·44	0·16	4·56	1·06	0·22	0·35
Rural Districts:— Percentage	0·27	4·85	1·56	0·26	0·44	0·30	4·47	1·14	0·23	0·37

5. Diet.—The nature of the diet as a factor in aetiology has been discussed by several investigators. Rendle Short (1920) attributed the increased incidence between 1895 and 1905 in this country mainly to changes in modern diet, with a reduction in cellulose and fibre content and its replacement by an increased consumption of imported foods, especially meat. In affirmation of this belief it has been stated that the disease is rare in primitive peoples living on native and predominantly non-protein diets; McCarrison (1922) did not meet with a single case among certain hill tribes in the Gilgil Agency, N. India, in nine years. Other observers have mentioned that it becomes quite common among Indians taking to a European meat-containing diet.

Mindful of the fact that there was a temporary decline in the mortality from diabetes at the older ages during the First World War—a decline ascribed to lessened food consumption—and that the statistical history of the mortality from appendicitis was similar in character, Young and Russell concluded that " the excess of food or possibly of certain types of food may play a part in the incidence of appendicitis ".

In view of this parallelism in the trends of the respective mortalities of the two diseases, it was of interest to assess their comparability during the Second World War. For this purpose the comparative mortality index was used. This index, which was introduced by Dr. Percy Stocks, " expresses the mortality of each year as a ratio to that of 1938, adopted as a base line, after adjustment for age differences in the population exposed to risk and for changes in cause assignment from 1940 onwards ". The figures compiled by the Registrar-General are given for biennial periods between 1934 and 1946 (*Table IV*).

Table IV.—Comparative Mortality Indices (Base Year, 1938)

Year	Appendicitis		Diabetes	
	Male	*Female*	*Male*	*Female*
1934–5	1·077	1·121	·992	·999
1936–7	1·034	1·029	1·049	1·044
1938	1·000	1·000	1·000	1·000
1939–40	·881	·850	1·076	1·041
1941–2	·706	·626	·931	·888
1943–4	·660	·672	·773	·785
1945–6	·559	·532	·653	·708

The figures reveal that the statistical history of the two diseases was quite different in the immediate pre-war period. The death-rates from appendicitis declined continuously between 1934 and 1940, whereas the mortality from diabetes was at a maximum in the latter year. Since then the death-rate from each disease has decreased, with the result that, in 1945–6, the mortality from appendicitis was approximately 45 per cent less than that in 1938, the comparable reduction for diabetes being approximately 30 per cent. This close accord in the movement of the respective rates of mortality might seem to indicate the influence of a common operative factor and, in this connexion, the ostensible causal influence would conceivably be the altered character of food consumption or the dietary balance. The hypothesis would, however, afford a sounder basis of argument if the statistics related to morbidity rather than to mortality. It would also apply with more justification to diabetes than to appendicitis, because there is no reason to suppose that in the war and post-war period diabetic patients were more careful or attentive to their needs in the matter of insulin therapy than in previous years, although its use may have been further extended in this period. As regards appendicitis, it must be recognized that factors other than diet—if diet be a correlate—have also tended to shape the gradient of the mortality. In recent years sulphonamides (and, later, penicillin) have aided the patients' recovery, and they have been used with increasing frequency. As a consequence of this fact it was of interest to predict the size of the mortality in 1946 on the basis of the secular trend between 1935 and 1940. The results were :—

Comparative Mortality Index

	Males	*Females*
Actual	0·507	0·497
Expected	0·584	0·521

The actual values are lower than the expected, but not appreciably lower. It would at least seem probable that the factors which have been specified are among those which have been responsible for the very appreciable decline in the mortality from appendicitis.

6. Mortality and Social Status.—The next aspect to which attention may be directed is the social distribution of the mortality, of which the relevant statistics have been compiled in the Registrar-General's Decennial Supplement, 1931, part 2A. For the present purpose the five officially identified social classes have been reduced to three by combining I and II to represent the best economic group; III the skilled workers; and IV and V the lowest social grade. The standardized mortality ratios which represent the actual deaths expressed as a percentage of the expected number, allowance being made for the age composition of the population, at age 20–65 years, males and married women, in the period 1930–2, were as shown in *Table V*.

Table V.—Standardized Mortality Ratios (S.M.R.) at Age 20–65 Years

Social Class (Group)	Males S.M.R.	Males Coefficient of Variation	Married Women S.M.R.
I and II	146	21	121
III	98	28	103
IV and V	78	19	83

It will be seen that there is an appreciable reduction in mortality, slightly more accentuated for men than for women, with descent in the social scale. For the men the range is from an excess of 46 per cent in Group I and II above the average for males to a defect of 22 per cent in Group IV and V. Although there is a definite demarcation between the mortality in the social classes, yet within each there is a remarkable uniformity as the coefficient of variation is 21 in Group I and II and 19 in IV and V, the lowest group. In other words, each occupation

or profession constituting Group I and II has, relative to the average, a uniformly high rate of mortality from appendicitis, while each in Group IV and V has a relatively low death-rate. The inverse relationship with social class is somewhat perplexing. In fact, the gradient is contrary to expectation since an important factor in appendicitis is bacterial infection, and diseases involving bacterial infection are generally more frequent among the poor. Undoubtedly the better-favoured sections of the community can consult and obtain the best medical advice more readily. This facility should lead to a better detection of cases. If varying efficiency of diagnosis be the explanatory factor, then one would expect that the social gradient in the mortality from a disease such as peptic ulcer should accord with that for appendicitis. But the direction or slope is entirely different as the death-rate from peptic ulcer increases with descent in the social scale. Hence it would seem that there must be some real cause to account for the higher mortality from appendicitis experienced in the upper ranks of society. Once again the dietary factor must be considered. The well-to-do, in ordinary times, consume higher quantities of meat and other protein foods and fat than the working classes. It may be possible that they are also more addicted to purgatives. It is conceivable that the products of protein digestion, given some mechanical reason for stasis in the vermiform appendix and altered fæcal consistencies, might provide a better medium for bacterial growth and so encourage inflammatory change. If the statistics of the mortality from appendicitis according to social status during the period of 'rationing' in this country had been available, they would be of much interest as they would help to shed some light on the part which diet plays in the causation of the disease.

7. Morbidity.—Apart from the information published by the Department of Health for Scotland in pre-war years, there are no published statistics of the incidence of appendicitis in the population generally. The Scottish data related to illness among the insured population. The evidence was based on the diagnosis made by general practitioners, and it may or may not represent a true picture, but it was the best available picture of the prevalence of the disease among people of certain age periods.

Since true, as distinct from suspected, cases of appendicitis to-day nearly always gain admission to hospital, it would seem that such admissions would afford an interesting field of inquiry. During the four years 1945–8 there were 1573 appendicular admissions to the Radcliffe Infirmary, Oxford, and, as will be explained later, 1074 (or 68 per cent), being regarded as acute cases, were made the basis of this section of our study. Before considering this clinical aspect the interesting question arises: what is the incidence of acute appendicitis among the general population? The statistics collected by the Nuffield Bureau of Health and Sickness Records at Oxford help to provide an answer of some reliability. For an area centring on the city of Oxford and containing twenty hospitals (the Radcliffe Infirmary is the largest) which serve a population of 300,000 persons the Bureau assembled particulars of 1710 appendicular admissions during the three years 1946–8. On the basis of the Radcliffe series, 68 per cent of these could be regarded as 'acute' cases. During the same period 78 acute cases were admitted to the main private nursing home in this area. Hence the total incidence of acute cases of appendicitis in this region during the three years in question was:—

$$1163 + 78 = 1241$$

which represents an annual case-rate of 1·38 per 1000 of the population. If this regional experience be regarded as representative of the country generally, then the annual number of acute cases in England and Wales is approximately 60,000, which means that 1 in every 700 of the population gets acute appendicitis annually.

II. ANALYSIS OF THE RADCLIFFE INFIRMARY SERIES

In this series every effort has been made to screen the case notes so that only those patients with an acutely inflamed appendix should be included. All operation notes and histological findings were jointly considered, and it was found that in almost all instances in which evidence of acute inflammation was doubtful at operation, the appendix had been submitted to histological examination. Any doubtful cases were discarded. 'Interval' appendicectomies were included only when the case was one where a mass had been present in the right iliac fossa or thereabouts, and subsequent findings at operation two or three months later provided sufficient evidence to show that appendicitis had previously existed. All cases treated conservatively in which such subsequent operative findings were not available were considered not proved and so discarded. From the records of this four-year period, 1573 case records labelled broadly 'appendicitis' were scrutinized. After excluding all cases labelled as 'chronic', 'subacute', 'appendicular colic', and all doubtful 'interval' cases, there remained 1074 histories for study in which proof of definite acute appendicitis was included. All patients were under the supervision of the staff surgeons, but, with the exception of 46, the operations were performed by the registrars, or occasionally by a house surgeon supervised by a registrar.

The 499 cases discarded merit consideration, and both from the clinical and social point of view they are of some importance. Many of these had, no doubt, had a true appendicitis at some time which had resolved, and the patients had come for removal of the appendix before a worse attack occurred. Such instances of previous mild attacks culminating in a more severe inflammatory episode are well recognized, and in the 1074 cases of proved appendicitis 363 patients (34 per cent) gave a history of one or more previous attacks of similar symptoms. In many of the discarded cases the appendices contained single or multiple fæcoliths of varying size; other appendices were badly kinked; a few harboured an argentaffinoma. All such defects may be considered as capable of producing symptoms and must, in some patients, have tended to undermine or disturb bodily health. In many other instances the appendices removed were normal and had probably never been otherwise. These serve, at least, to remind us that in the diagnosis of conditions giving rise to abdominal

pain we have a lot to learn, and that there could be much saving of beds, costs, and surgical time, and of anxiety for patients and relatives, if the safety of appendicectomy had not in some measure hampered the growth of clinical judgement.

1. Age Distribution.—The age distribution of the hospital patients is recorded in *Table VI*. There were 29 per cent under age 15, and 63 per cent between the ages of 15 and 55 years. When the age composition of the sexes was compared, it was found that a significant difference existed—there being proportionately more females than males in the higher age groups. The value of P—a test of the significance—was found to be less than 0·01. This implies that the observed differences between the respective age distributions of the two sexes would occur less than once in a hundred times by mere chance. Of course this disparity may represent nothing more than a corresponding disproportion in the unknown age distribution of the population exposed to risk.

Table VI.—Age and Sex Distribution of Patients with Appendicitis admitted to the Radcliffe Infirmary, Oxford, during the Period 1945–8, inclusive

	Age Groups					
	0–4	5–14	15–54	55+	N.S.	All Ages
Males	25	172	352	41	1	591
Females	8	105	324	45	1	483
Persons	33	277	676	86	2	1074
Percentages						
Males	4·2	29·1	59·6	6·9	0·2	100
Females	1·7	21·7	67·1	9·3	0·2	100
Persons	3·1	25·8	62·9	8·0	0·2	100

2. Types of Case and Frequency.—In order to study the results in cases of varying severity, the system of grouping used by Grey Turner (1938) was chosen as a highly suitable one. It is more definitive than the system used by the Medical Research Council (1944) and, though not so detailed as that suggested by Wevill and Wallace (1934), it is more readily adaptable to such information as the case-history commonly provides. Grey Turner's system of grouping was as follows :—

Group 1. Acute appendicitis without peritonitis.
Group 2. Acute appendicitis with localized peritonitis.
Group 3. Acute appendicitis with flank or pelvic peritonitis, or both.
Group 4. Acute appendicitis with diffuse peritonitis.
Group 5. Acute appendicitis with residual abscess.
Group 6. Acute appendicitis with primary localized abscess.
Group 7. Acute appendicitis with interval removal.
Group 8. Acute appendicitis with primary complications.
Group 9. Acute appendicitis with no operation.
Group 10. Appendicitis with incidental removal.

The percentage of the total cases which occur in each category for each sex is stated in *Table VII*. Group 10 (incidental removals) is not considered in this series. There is no apparent difference between the percentages for males and females within each category. The most frequent type of case was that represented by Group 1—appendicitis without peritonitis—which contained 39 per cent of the total male series and 43 per cent of the total female series.

The proportion of cases with peritonitis (Groups 2, 3, 4) amounted to 48 per cent for males and 45 per cent for females, and the incidence of abscess (Groups 5, 6) was 10 per cent for males and 9 per cent for females. Only 4 cases are classified in Group 9 (no operation). These were subsequently proved by operation to be instances of true appendicitis presenting with appendicular abscesses, but the subsequent operation was performed outside the time-limits of this study.

The age distribution of males and females within each group was compared, and it was found that there was a possible difference in Groups 1, 2, and 6 which, when tested for significance, gave the following results :—

Group 1 (acute appendicitis without peritonitis)	'P' less than 0·001
Group 2 (acute appendicitis with localized peritonitis)	'P' greater than 0·05
Group 6 (acute appendicitis with primary localized abscess)	'P' lies between 0·01 and 0·02

Table VII.—Frequency of Type of Appendicitis, according to the Grey Turner Classification, among Cases admitted to the Radcliffe Infirmary, Oxford

Grey Turner Classification	Males	Per-centage	Females	Per-centage	Total Persons	Per-centage
1	232	39·3	208	43·1	440	41·0
2	161	27·2	117	24·2	278	25·9
3	66	11·2	63	13·0	129	12·0
4	58	9·8	39	8·1	97	9·0
5	4	0·7	—	—	4	0·4
6	55	9·2	42	8·7	97	9·0
7	12	2.0	11	2·3	23	2·1
8	1	0·2	1	0·2	2	0·2
9	2	0·3	2	0·4	4	0·4
Total	591	100	483	100	1074	100

Hence it can be stated that the sex difference in the age distribution, previously indicated in *Table VI*, was largely influenced by the statistical experience of Group 1. In the other categories there was no pronounced disparity, although the result in Group 6 indicates a borderline significance.

3. Case Fatality in Each Group.—The operation notes generally provided sufficient information to make possible a correct grouping in respect of the severity of inflammation; in the few doubtful instances the case was placed in the less advanced group. *Table VIII* gives the details. A comparison is made with the figures of a personal series of Grey Turner's (1938) for a thirty-four-year period to the end of 1934. This latter series is closely comparable in numbers with the present one. The results in Grey Turner's series are broadly representative of many other series covering the second and third decades of the century, as detailed in the M.R.C. Report of Young and Russell (1939). Cases of interval removals are excluded from both series owing to differences of interpretation.

Table VIII.—Case Fatality according to Type of Case

Present Series				Grey Turner's Series			
Group	*No. of Cases*	*Deaths*	*Percentage Case Fatality*	*Group*	*No. of Cases*	*Deaths*	*Percentage Case Fatality*
1	440	—	—	1	159	—	—
2	278	4	1·4	2	428	4	0·9
3	129	2	1·6	3	230	22	9·6
4	97	6	6·2	4	96	28	29·2
5	4	—	—	5	64	5	7·8
6	97	1	1·0	6	446	16	3·6
8	2	2	100·0	8	20	9	45·0

The present series shows a case fatality not higher than 1·6 per cent in any group, except in Group 4 (general peritonitis) where it is 6·2 per cent in 97 cases, whereas in Grey Turner's 96 cases of general peritonitis the fatality was 29·2 per cent. Little importance can be attached to the fatality in Group 8 because it is based upon 2 cases only. Surgical detail has altered little in the interval between these two series. Infusion and transfusion therapy, together with some other factors considered below, may have had some influence in this great reduction of mortality, but there can be no question that the saving of life and lessening of morbidity have been chiefly brought about by modern chemotherapy.

4. Delay in Operating.—The cases were broadly divided into those operated on before or after 48 hours from the onset of symptoms. In 47 the history was defective. Of the 1027 cases in which the necessary information was available, 75·5 per cent were operated on within 48 hours, and a further 7·5 per cent were under surgical supervision in the same time, but operation was delayed for special reasons. It is to the credit of practitioners and the transport services, especially since many patients came from rural districts, that 83 per cent were in the surgeon's hands within 48 hours of the onset of symptoms. There is, however, no cause for complacency, for of this 83 per cent as many as 25 per cent were already in the severe Groups 3, 4, 5, 6. Of the 17 per cent treated later than 48 hours, as many as 57 per cent were in the same severe groups. In 143 cases (14 per cent) delay was greater than 72 hours, *and in the 15 fatal cases all but 3 showed a delay of over 72 hours.*

It is of even greater import to note that among those 480 patients giving a history of less than 24 hours there were 46 with flank or pelvic peritonitis, 25 with general peritonitis (1 death), and 9 with localized abscess. We are reminded of J. B. Murphy's caution, given as long ago as 1916, that "early operation is the only safe practice". Early operation depends upon early suspicion, a better recognition in the field of practice of the various modes of onset, and prompt reporting of symptoms by patients. But the stages of the disease process in appendicitis are only roughly proportional to the length of symptoms, and we must expect to see many cases with symptoms of only a few hours' duration but who have gangrenous or even perforated appendices. Thus, in this series, in 164 cases the history was alleged to be less than 12 hours, and 22 of these cases were already in Groups 3 or 4. *It is dangerous to delay even when the symptoms have been present for only a few hours.*

5. Incision.—This information was available in almost every instance and of stated cases a laterally placed incision (R.I.F.) was used in 86 per cent, and a centrally placed (median, paramedian, and Battle) in the remaining 14 per cent. For patients with general peritonitis a centrally placed incision was used in 31 per cent of cases. This high figure might appear to indicate that the abdomen was being opened rather frequently on an uncertain diagnosis of the cause of the peritonitis. It may be suggested that, whenever possible, a laterally placed incision is a better one, as it leads to less intraperitoneal handling and disturbance; subsequent adhesions of the cæcum to the wound are more common with such an incision. With a central incision adhesions involving the small bowel, with a great liability to future obstruction, are also more common. But the best incision is over the site of the appendix, and when this is deemed to be central the incision should be likewise. In cases with general peritonitis it is usually preferable to make an initial small incision laterally if there is a reasonable chance of the cause being appendicitis and, when this is not the case, to incise again over the appropriate site. Eighty cases in Groups 1 and 2 had centrally placed incisions, which also seems an unduly high figure. As 50 of these latter cases were females, it would appear that the distinction of appendicitis from disease of the

female pelvic organs is ever a difficulty, and, in fact, the gynæcologists removed some acutely inflamed appendices and the general surgeons had a share of the ectopic gestation cases.

6. Removal of the Appendix.—In almost all cases the appendix was treated by ligature and invagination of the stump, but occasionally this step was described as " not possible ". Personal preference (G.E.M.) is for ligation and double invagination, thus treating the appendix stump with much the same respect as that of the duodenum in a Polya gastrectomy. Few would have the temerity to leave a duodenum occluded by one ligature, and yet the stresses operating in the colon and the duodenum are not dissimilar. When a duodenal stump leaks the disaster is obvious and the surgeon is usually willing to blame himself. When an appendix stump leaks complications are commonly considered to be due not to a ' blown stump ' but to a ' residual abscess ', and an effect of chance rather than of imperfect surgery.

When the appendix has ruptured at its base, the cæcal wall may be like thick, wet blotting-paper, with perhaps a gaping hole into its lumen. It is appropriate to recall the lesson of war surgery that it is better to anticipate the fæcal fistula by draining a perforated colon to the exterior ; the colon does not differ in its subsequent reaction to perforation, whatever the cause of the hole. In such cases it is better to insert a tube through the defect into the cæcum and to suture the available tissues about it with a wide purse-string. Four such cases were thus treated in this series with satisfactory results. A fæcal fistula may also arise from other factors, such as sloughing of the wall of the bowel adjacent to an abscess, or to a mesenteric thrombosis. There were twelve instances of fæcal fistula in this series, three being in fatal cases. The time-worn optimistic surgical adage that " fæcal fistulæ do well ", which applied more to spontaneous relief of an obstruction, is unsound teaching, though perhaps a solace to a distressed and disgusted patient. A better catchphrase might be " fæcal fistulæ are best anticipated ", and so safely established and directed by the surgeon.

A procedure commonly recorded in the operation notes was that pus and turbid exudates were sucked out of the peritoneal and pelvic cavities. The application of pure carbolic to the appendix stump appeared from the notes to have been performed so erratically that there seemed little faith in its use. Deficient records on this point made precise analysis impossible. The appendix was not removed in a few instances on grounds of difficulty and the poor condition of the patient. There was one such instance in the fatal cases in which operation was performed.

7. Chemotherapy.—

a. Sulphonamide.—Local use of sulphonamide powder in the wound and peritoneal cavity, with or without penicillin, was recorded in 513 of the cases and avoided in 531. In severe cases it was used more frequently, although in 63 such cases it was not employed. Sometimes it was dusted into the peritoneal cavity as well as the wound. Surgeons appeared to differ in their reliance upon these methods. From the detailed analysis the only conclusion is cited below in connexion with wound sepsis.

Systemic sulphonamide was used in a variety of preparations, by mouth when possible, and if not possible mostly as sodium sulphathiazole by injection (I.M.) 4-hourly. Its use was largely confined to severe cases, although 194 cases in Groups 1 and 2 were recorded as dosed, as compared with 524 which were not. Lack of conviction or omission resulted in 32 cases in Group 3, 4 in Group 4, and 19 in Group 6 going without chemotherapy. In the 15 fatal cases 3 received no sulphonamide and only 2 cases received a heavy dosage. In order to study the strength of dosage the cases were analysed into the arbitrary figures of small (1 g., or less, 4-hourly), moderate (2 g. stat., followed by 1 g. 4-hourly), and heavy (above 2 g. stat., followed by 1 g. 4-hourly). The overall findings can be instanced by the general peritonitis cases, in which the distribution of dosage was small in 14, moderate in 54, and heavy in 24.

The early plea expressed by Corry, Brewer, and Nicol (1939) for the use of sulphonamides in appendicitis has undoubtedly been justified, and the great lowering of mortality and morbidity must largely be due to this aid.

b. Penicillin.—This was used sparingly during 1945, but in the last three years its use was much more general. It was given mostly by single injection (I.M.) 3- or 4-hourly. Dosage was analysed, as with sulphonamide, into small (below 10,000 units 3-hourly), moderate (10,000 to 20,000 units 3-hourly), and heavy (over 20,000 units 3-hourly), and the general tendency was to use the heavier dosage relatively more commonly than in the case of the sulphonamides, although 6 cases of general peritonitis received only moderate dosage. But the use of penicillin was withheld more frequently than was that of the sulphonamides, 41 cases in Group 3, 26 in Group 4, and 21 in Group 6 receiving none. In 2 of the fatal cases penicillin had not been used, and in a further 2 its use was withheld till the patients were desperately ill. The scale of dosage detailed above might now be considered generally low, but it was according to the general standard during the period relating to this series.

The general impression gained from the dosage tables of both sulphonamides and penicillin is that they were employed with insufficient frequency and, when employed, that the dosage was commonly too small. Further observations on chemotherapy are made below.

8. Residual Peritoneal Abscess.—A total of 40 instances of this complication was recorded, the details being shown in *Table IX*. The types of chemotherapy which these abscess cases received are detailed in *Table X*.

The incidence of residual abscess is seen to be low, and it is particularly gratifying that only one subphrenic abscess developed in the whole series. It will be noted that almost all these cases received sulphonamides systemically after operation, and the majority were given both penicillin and sulphonamide. In spite of this therapeutic aid the occurrence of 40 abscesses was not prevented. Although adequate dosage was given to the majority of these abscess cases, the general impression from the dosage tables of both sulphonamide and penicillin is that in too many cases in which a residual abscess resulted, the dosage of both drugs had been too low. In the

management of these residual abscesses conservatism was usually adopted, and most discharged spontaneously into the bowel lumen, through the wound, or 'resolved'. Only occasionally was surgery used for their evacuation.

Table IX.—Residual Peritoneal Abscesses

Site	No. per Group			
	Group 2	*Group 3*	*Group 4*	*Group 6*
R.I.F.	2	5	4	–
Pelvic	3	2	14	9
Subphrenic	–	–	1	–
Total	5	7	19*	9

Table X.—Relation of Residual Peritoneal Abscess to Chemotherapy (Cases)

Type of Chemotherapy	No. per Group			
	Group 2	*Group 3*	*Group 4*	*Group 6*
Penicillin post-operative	2	6	13	7
Sulphonamide post-operative	2	5	17	7
Sulphonamide at operation	4	3	12	8
No. with any combination	5	7	18*	9

* Discrepancy due to two abscesses in one case

9. Drainage.—There was a time when this question was not at issue. "Better a drain than a coffin" left no uncertainty in the junior's mind what to do about it. The reawakening of criticism has come only with the advent of modern chemotherapy. In this series are found 17 cases in Group 1 where peritoneal cavities were drained. They suffered no harm. Nor did 423 patients, also in Group 1, whose peritoneal cavities returned to normal without the influence of rubber tubing.

Differences of opinion on this point exist in many centres, as in that from which these cases are collected. In this series it has been possible to classify the results under two main categories of practice: (i) in which a drain is used fairly freely, but by no means always; and (ii) in which a drain is very seldom employed. The cases in this series are classified according to drainage (*a*) of the peritoneal cavity, (*b*) of a localized abscess, and (*c*) of the wound. In some instances a case has been treated by a drain at all three points. The details of cases in categories (*a*) and (*b*) and of those who had no drainage are shown in *Tables XI, XII, XIII.*

It might be asserted that drainage had evidently been used in the worst peritonitis or abscess cases and that closure was reserved for those with less serious inflammatory complications. With most operators this was the case, particularly in the earlier period covered by the survey. Latterly the cases under one surgeon have had drainage greatly reduced, so that in 22 instances of abscess (Group 6) of all types, only in 2 cases was a drain used. In 34 instances a drain was placed, not intraperitoneally, but in the layers of the abdominal wound; the discussion on this procedure is relegated to the section on wound sepsis.

The number of fatal cases in this series is very small, so that it is difficult to assess the comparative values of drainage in this respect, but in those 10 cases in which the question of drainage could possibly have had time to apply or to be pertinent in any way, as many as 7 had peritoneal drainage. One case in Group 2 died without a drain or chemotherapy.

It will be observed from *Table XI* that in Groups 3 and 4 together, drainage of the peritoneal cavity in 112 cases was followed by abscesses in 13; in the same groups where no drainage was used (*Table XIII*), 106 cases were followed by abscesses in 10. Where a localized abscess was drained (*Table XII*), 41 cases gave 8 (20 per cent) residual abscesses, whereas in 44 undrained cases of localized abscess only 4 (9 per cent) residual abscesses resulted. This suggests an appreciable reduction of residual abscesses when drainage was avoided, but the difference is not statistically significant; nor is it possible to make allowances for other factors which may have influenced results in the two series. It is tempting to assume that the problem of drainage in appendicitis is a different one from that of drainage of abscesses occurring in other parts of the body. There is no sound evidence that such is the case. All who have experienced the impossibility of draining the last few pints of an ascites by a stab drain into the pelvis must accept that better success is unlikely when the fluid is thick and loculated. Little will pass through the layer of fibrin which rapidly forms about a drainage tube. Before the advent of chemotherapy, it was possibly the wisest measure to leave a drain into an abscess which had been evacuated, but we must review the situation now that it has been so much changed by chemotherapy. In lesions other than appendicitis the change of principle has been admirably demonstrated in cases of bone infection by Trueta and Agerholm (1948), and in infections of the hand by Louden, Minero, and Scott (1948). Both these papers have described techniques in which purulent infection is attacked directly, the debris cleared out, a chemotherapeutic agent introduced, the wound closed, and subsequent adequate chemotherapy is instituted. Only in long-standing thick-walled abscesses affecting these parts or tissues is it considered necessary to employ drainage. In most of the undrained appendix abscesses in this series this principle was followed, and with a comparable improvement in results. Green and Watkins (1946) have also shown a reduction in mortality when drainage is reduced. Some incidental findings illustrating the uncertain functioning of drainage are illustrated by two cases in each of which an abscess in the R.I.F. was drained, but a pelvic abscess followed in both instances. In two other cases an abscess in the R.I.F. developed after the drainage tubes were removed from the R.I.F. Extending experience is leading to a decline in the use of multiple drains. They have not stood the test of time, and even with the use of a single drain it is well known that an abscess may form at points distant from the original abscess. Since closure without drainage and employing chemotherapy would appear to result in

fewer residual abscesses, the case for a departure from older orthodox practice would now seem to have support. But the use of a drain is probably still advisable in some conditions which are listed below :—

1. In an adherent retrocæcal appendix when tissue planes may be widely opened, with resultant oozing from multiple points, it may be difficult before closure to prevent the formation of a pool of blood. Such a local collection of blood is not infrequently the precursor of an abscess; it is probably best treated by removing as much as possible by a stab drain to the site for 24 hours.

2. A chronic, well-localized, thick-walled abscess will probably benefit by the presence of a drainage tube. In a few such cases there may be a re-accumulation without the use of a drain. But if the walls of such an abscess have been broken in seeking for the appendix, a drain is probably best avoided. A few residual abscesses will develop whether or not a drain is used, and if the drain is avoided there will probably be less abscesses with quicker and sounder wound healing.

3. The use of cæcostomy in cases where the base of the cæcum is perforated has already been mentioned.

Table XI.—Drainage of Peritoneal Cavity

Group	No. Drained	Site of Abscess			Total Abscesses	Abscesses Percentage Drained
		R.I.F.	*Pelvic*	*Subphrenic*		
1	17	—	—	—	—	—
2	66	1	2	—	3	5
3	57	1	—	—	1	2
4	55	2	10	—	12	22
5	1	—	—	—	—	—
6	10	—	1	—	1	10
7	—	—	—	—	—	—
8	1	—	—	—	—	—

Table XII.—Drainage of Abscess

Group	No. Drained	Site of Abscess			Total Abscesses	Abscesses Percentage Drained
		R.I.F.	*Pelvic*	*Subphrenic*		
4	4	—	2	—	2	50
5	3	—	1	—	1	33
6	41	2	6	—	8	20

Table XIII.—No Drainage

Group	No. Not Drained	Site of Abscess			Total Abscesses	Abscesses Percentage
		R.I.F.	*Pelvic*	*Subphrenic*		
1	423	—	—	—	—	—
2	207	1	1	—	2	1
3	68	4	2	—	6	9
4	38	1	2	1	4	11
5	1	—	—	—	—	—
6	44	2	2	—	4	9
7	22	—	—	—	—	—
8	1	—	—	—	—	—

10. Bacteriological Findings.—All records were searched for data on this aspect, but statistical analysis was not possible owing to many omissions. It was found that a swab was taken at operation in the majority of cases with severe infections and with a local abscess. In the direct smears the common findings were Gram-negative rods, Gram-positive cocci, and, not infrequently, actinomycotic filaments. In the cultures *B. coli* was the commonest finding, often alone but frequently with *Str. fæcalis*. Sometimes anaerobic streptococci were present, and less frequently *Cl. Welchii*. Often the swabs were sterile on culture. Some other flora of an interesting nature were brought to light. In two instances beta-hæmolytic streptococci were found in swabs of pus taken at operation, and in another case the same organism was grown in pure culture from pus in a pelvic abscess found at necropsy. A swab from a residual peritoneal abscess which was incised showed *Staph. aureus* on culture; this may have been an introduced infection.

It is acknowledged that the organisms found in appendicitis and resulting peritonitis range from the virulent and moderate invaders to the less harmful secondary infectors and the harmless saprophytes. Some strains of the *Str. fæcalis* or the anaerobic streptococci, for example, are more virulent than others. Some are sensitive to sulphonamides but insensitive to penicillin, and the reverse can also be true. Without elaborate laboratory techniques, proof of virulence and sensitivity remains unknown. Should the appendicitis victim have an infected mouth or throat, beta-hæmolytic streptococci, *Staph. aureus*, actinomyces, and other organisms may be in abundance in the bowel contents, including the lumen of the appendix at the moment when inflammation is initiated, and they may take part in that inflammation. The inference from these observations is that we cannot know which of the many possible organisms are active in any one case at the crucial initial stage. It is thus rational to assume the worst and institute powerful chemotherapy in all cases where infection has passed beyond the boundary of the appendix itself. Support for this view is found in *Table IX* which shows that there were no instances of residual abscess in Group 1, but that in Group 2 there occurred 5 instances. Since some of the organisms are penicillin-sensitive and sulphonamide-resistant, and vice versa, both drugs should logically be used from the start. It has now become necessary to consider the additional use of streptomycin or other antibiotics. Streptomycin was not available during the period under review, but it is now mostly reserved in the Radcliffe Infirmary for cases in or worse than Group 3.

11. Wound Infections.—The bacteriology of the wound infections provided some interesting data. In comparatively few cases of this complication were repeated swabs examined, but among the recorded instances were found 10 of infection with *Staph. aureus*, 3 with beta-hæmolytic streptococci, and 2 with actinomyces. The total number of infections with these virulent organisms was probably higher. No matter what the origin of these organisms

may be, the facts indicate that routine cultures from wound discharges should be made, and when virulent organisms are found, the appropriate chemotherapy should be employed.

12. Wound Healing (including relation to suture materials).—The high mortality which has been associated with appendicitis until this decade has tended to thrust the question of wound sepsis into the background as a frequently unavoidable incident. But with a saving of life in almost 99 per cent of cases, attention should now be turned to the reduction of post-operative morbidity.

Ideal healing is seen in a wound which is closed at operation and which gives no further trouble. Possible adverse factors to wound healing include the presence of bacteria, blood-clot, suture material, drainage tubes, and chemicals. A definition of wound 'infection' remains to be established. For example, all wounds in cases of peritonitis are infected, but only some become clinically inflamed. All wounds which contain a drainage tube for a week are bound to be invaded by organisms of some sort, and many wounds in this period become reddened and slightly swollen; no instances of this nature have, however, been included in this series as examples of wound infection. The standards chosen were: (*a*) discharge of pus from a closed wound; (*b*) discharge after ten days from a wound in which a drainage tube is or has been situated; and (*c*) discharge of suture material from a wound. This last incident might not be considered as evidence of 'infection' on all occasions, but as it is a manifestation of incomplete healing and is a 'discharge' from a wound, it is placed for convenience in this category and is also included in the total figures for sepsis in each section of *Table XIV*. Owing to inadequate information in the case records, it was not possible to assess the frequency of 'stitch' abscess, and no instances of wound infection refer to this condition.

In an analysis of wound healing, the various factors aiding or preventing healing should be taken into account and like should be tested against like, if possible. Detailed analysis was made of the employment of sulphonamide and penicillin powder in the wound, at operation and post-operatively, alone and together, and the mode and frequency of use were analysed in relation to wound disturbance. But the single or combined use of these substances was so inconsistent that no true statistical conclusions are possible. The use of catgut and nylon sutures provided other variables. Although in some cases both penicillin and sulphonamide were used both locally and systemically, wound troubles developed. In the catgut series, in the 60 cases of wound disturbance in Group 2, some 30 cases had local and general treatment with both drugs; and in the nylon series, in the 6 cases in Group 2 with wound troubles, 4 cases had the same types of chemotherapy.

Hæmatomata are well recognized as interfering with healing. The case notes rarely indicated that a hæmatoma had formed in a wound, and the point was not specifically analysed. The occurrence of hæmatomata was suggested in some cases by the description in the notes of "a discharge of blood and pus". Prevention of hæmatomata is, of course, important, but it is a standard surgical detail calling for no further comment here.

There remains the study of the influence on healing of suture material, and of drainage tubes which traverse or are placed in the layers of the wound. Suture with tantalum, steel wire, and thread were used as a trial in less than 10 cases and are not further considered here. All other wounds were sutured with catgut or nylon, and the detailed analysis with the relation to sepsis is shown in *Table XIV*. There are some slight discrepancies in the totals owing to both nylon and catgut being used in some few cases, as well as some cases of abscess being treated by interval appendicectomy.

The severity of wound infection was graded into mild and marked, and analysed for those cases sutured with catgut or nylon. It was found in the series with catgut that 17 per cent of infections were mild and 6 per cent marked; in the series with nylon there were 5 per cent mild and 5 per cent marked.

If chemotherapeutic factors are excluded and consideration given only to the analysis of wounds sutured by catgut or nylon, there is found to be a distinct balance in favour of the wounds sutured by nylon. A considerable portion of the sepsis in the catgut series is due to infection occurring about the site of a drain. Drainage was used in 28 per cent of all cases in which catgut was the suture material, and in only 15 per cent of all cases sutured with nylon. Apart from any useful purpose which the drains may have served, they would appear to have an adverse effect on wound healing. This is understandable when one recalls the experience of war surgery, which taught that wounds heal better when foreign material is excluded from them. Some surgeons, in cases of peritonitis, still prefer to close the peritoneum alone, while leaving the other layers of the wound widely open; but to do this is to

Table XIV.—A Comparison of the Incidence of Sepsis in Wounds sutured either with Catgut or with Nylon

		Group							
		1	2	3	4	5	6	7	8
All cases	No. of cases	440	278	129	97	4	97	23	2
	Percentage with wound sepsis	7	23	28	40	50	35	44	100
Catgut cases	No. of cases	336	208	83	64	2	42	13	2
	Percentage with wound sepsis	8	28	37	50	50	60	—	—
	Percentage with sepsis of closed part of wound	6	13	11	11	50	12	—	—
	Percentage with sepsis at drainage site	1	10	18	30	—	31	—	—
	Percentage with late discharge of suture	2	5	8	9	—	17	—	—
Nylon	No. of cases	119	70	49	35	1	30	10	—
	Percentage with wound sepsis	3	6	10	10	100	30	10	—
	Percentage with sepsis of closed part of wound	2	—	8	9	100	7	—	—
	Percentage with sepsis at drainage site	—	6	—	9	—	23	10	—
	Percentage with late discharge of suture	1	3	2	3	—	—	10	—

disregard another lesson from war experience—which is that most infected wounds will heal satisfactorily when closed with chemotherapeutic support. In the nylon series 5 out of 6 of the wounds in the severe groups healed by first intention, and infection was serious in only one-ninth of those patients who developed wound sepsis. It is a heavy penalty to the many patients whose wounds may be expected to heal soundly to abandon all faith and suture none. It has already been shown that the peritoneum is not materially assisted in its work in most cases by a drain; its presence in the wound can also be an embarrassment to sound healing. A wound will be assisted in healing by omitting the drain which some elect to place in its layers in cases of peritonitis. Such a drain was used 34 times in this series.

Stitch troubles, with later discharge of sutures, are much more frequent with catgut than with nylon, and from the operation notes it appeared that in several instances the trouble was due to subcutaneous suturing and ligaturing which left sutures close to the skin. The preference of one of us (G.E.M.) in cases more severe than Group 1 is for two or three mattress sutures of nylon, gently tied, which include the superficial and deep layers of fascia, and are subsequently removed. In 4 cases nylon sutures were removed in out-patients from sinuses which then healed. In 2 cases it was necessary to remove nylon sutures by opening the wound to a small extent under anæsthesia. Both these cases had had prolonged drainage, and the sinuses would not heal until the sutures were removed.

13. Other Complications.—The type and frequency of these are detailed in *Table XV*.

Fæcal fistula has already been considered. *Pulmonary complications* were not high, and only 1 case of pneumonia proved fatal—that of an infant admitted with both pneumonia and appendicitis. Good anæsthesia and careful pre- and post-operative attention have kept this source of trouble at a low level. Other lesser pulmonary complications included cough without physical signs, and mild 'bronchitis' which was not labelled under atelectasis in the notes. Several of the pulmonary complications were probably due to small emboli, but no cases of emboli below the level of the 'femoral' were recorded. Probably early mobilization of the patient has reduced this complication, but modern investigations on this point suggest that the occurrence of lesser degrees of thrombosis with small complicating embolisms is a more frequent occurrence than this investigation has revealed. *Femoral thrombosis* occurred in 6 cases, but only 2 cases of severe *pulmonary embolism* were found, 1 with hæmoptysis, and the other with sudden death from massive embolism. *Paralytic ileus*, as might be expected, was found chiefly in the peritonitis group, in which 16 cases were recorded, although it is likely that several instances of more moderate degree escaped record. In 8 of the fatal cases, paralytic ileus was marked. Occasionally the Miller-Abbott tube was used, but in no case was operation resorted to in the treatment of ileus. *Mechanical intestinal obstruction* was infrequent. To this, it is not unlikely that quicker and more complete resolution after chemotherapy contributed. These cases were treated by operation, and 3 of the 6 cases died. Two of the fatal cases were treated by ileostomy. *Further operations* included operation for obstruction, for drainage of residual abscess, or for resuture of broken-down wounds. *Other complications* included such

Table XV.—OTHER COMPLICATIONS

	Group								
	1	2	3	4	5	6	7	8	Total
Fæcal fistula	1	1	2	7	1	—	—	—	12
Pulmonary:									
1. Atelectasis	7	2	1	7	—	4	—	—	21
2. Pneumonia	2	2	1	4	—	2	—	1	12
3. Other	6	8	1	3	—	1	—	—	19
Paralytic ileus	1	2	6	16	—	3	1	—	29
Mechanical intestinal obstruction	—	2	1	3	—	—	—	—	6
Further operation	2	2	5	6	—	2	—	—	17
Femoral thrombosis	1	1	1	2	—	1	—	—	6
Pulmonary embolus	1	1	—	—	—	—	—	—	2
Other	7	14	9	11	—	2	—	—	43

various items as conjunctivitis, retention of urine, herpes labialis, diarrhœa, and symptomless persistent post-operative pyrexia. Concurrent diseases were found in 140 patients.

14. Infusion Therapy.—An intravenous drip was used in 58 patients, and only 6 of these were in the milder Groups 1 and 2. It was gratifying to find that only in 35 of 98 cases of general peritonitis was an intravenous drip used. Many patients with peritonitis who do not develop ileus will absorb fluid perfectly well by mouth with no discomfort or risk. The majority of the others can be tided over by rectal or intramuscular saline at no risk and little inconvenience, and by this means much discomfort and possible painful venous thrombosis is avoided, together with other attendant evils such as pulmonary œdema. When other means fail, it is, of course, essential to use the veins. If parenteral therapy was necessary, it was usual in this series to keep the stomach or intestines aspirated by an oral or nasal tube, but sometimes infusions were a means of augmenting a limited oral intake.

15. Length of Stay in Hospital.—An attempt was made to determine the length of patients' stay in bed, but information on this point was so scanty that no analysis was possible. The length of time in hospital was fully analysed and it is evident that all surgeons were striving for a short stay for their cases, and as many as 110 patients in Groups, 3, 4, and 6 had left the hospital by the tenth post-operative day. Thirty-eight of the 98 patients with general peritonitis were still in hospital after eighteen days. The effect of drainage on length of stay was analysed, the number of patients leaving hospital by the twelfth day being taken as a standard. For Groups 3 and 4 together, about half the patients had left hospital by that time whether or not a drain was used. In the case of abscess, 36 per cent of patients treated with drainage and 77 per cent of patients treated without drainage had left hospital by the twelfth day.

16. Convalescent Home.—This was used for 28 per cent of patients and the proportion in each group was much the same as for the total, except for cases of general peritonitis, where it was 42 per cent. The chief purpose of transfer to a convalescent home

was to make beds available in the parent hospital, and cases were transferred as beds happened to become available with suitable cases to go into them; the more serious cases were given preference where possible, as the figures for the peritonitis cases showed. An analysis of these patients by social classes showed no preference in this respect.

contained in the reports of the Registrar-General for England and Wales during the period 1920 to 1946; the morbidity related to the admissions with acute appendicitis to the Radcliffe Infirmary, Oxford, during the four years 1945 to 1948.

From this study the following conclusions are warranted :—

Table XVI.—Fatal Cases

No.	Group	Sex	Age	Duration of Symptoms (Hr.)	Post-operative Life (Days)	Drainage at Operation	Cause of Death	Comment
1	2	M.	63	72	11	No	Pelvic abscess, paralytic ileus, acute hæmorrhagic pneumonia	β-hæmolytic strep. in pelvic pus at P.M.
2	2	F.	15	30	6	No	General peritonitis, paralytic ileus	Appendix ruptured during delivery. No penicillin. No bacteriology
3	2	M.	16	96	11	No	Pelvic abscess, paralytic ileus, mechanical intestinal obstruction, second operation of jejunostomy (7th day)	No penicillin or sulphonamide till after second operation
4	2	F.	52	100	5	No	Thrombosis R. iliac vein, massive pulmonary embolism	Progress satisfactory until onset of embolism
5	3	F.	35	48	17	Yes	R.I.F. abscess, paralytic ileus, mechanical intestinal obstruction, second operation of ileostomy (16th day)	No sulphonamide till day of second operation
6	3	M.	55	144	20	Yes	Fæcal fistula, paralytic ileus, periappendicular cellulitis, bronchopneumonia, focal suppurative nephritis	Base of appendix ruptured. No cæcostomy
7	4	M.	63	72	35	Yes	Fæcal fistula, paralytic ileus, mechanical intestinal obstruction, second operation for closure of fæcal fistula and ileotransverse colostomy (33rd day), bronchopneumonia	Appendix not removed. Extensive secondary operation
8	4	M.	70	336	1	Yes	Severe general peritonitis	Very poor condition on admission. Did not rally from operation
9	4	M.	21	72	1	No	Severe general peritonitis	Very poor condition on admission. Did not rally from operation
10	4	M.	15	96	—	—	Severe general peritonitis	Condition too weak for operation
11	4	F.	12	240	16	Yes	General peritonitis, pelvic abscess, fæcal fistula	Advanced disease on admission. Abscess drained after 11 days in hospital
12	4	M.	56	96	11	Yes	R.I.F. abscess, general peritonitis, paralytic ileus	Advanced peritonitis. No penicillin until 9th day
13	6	M.	11	72	53	Yes	Appendix abscess drained, abscess of abdominal wall (incised 1 month later), abscess of L.I.F. (incised 2 months later), portal pyæmia with multiple liver abscesses, subphrenic abscess, and suppurative pericarditis	No penicillin
14	8	F.	78	24	9	Yes	Myocardial degeneration, operation for a Group 2 type of appendicitis	Cardiac failure on admission
15	8	M.	1	72	3	Yes	Bilateral bronchopneumonia, operation for appendicular abscess	Being treated for pneumonia before admission

17. Fatal Cases.—*Table XVI* serves to illustrate the adverse influence of youth and age, of delayed admission to hospital, of mechanical obstruction and the need for secondary operations, and of acute complicating emergencies such as embolism.

III. SUMMARY AND CONCLUSIONS

In this investigation the social pathology and recent surgical experience of appendicitis have been considered. The mortality was based on the data

1. There are probably some 60,000 cases of acute appendicitis (or approximately 1 in 700 of the population) occurring in England and Wales each year.

2. In 1946 there were 867 deaths from this cause among males and 668 among females.

3. The secular trend of mortality between 1920 and 1946 has been satisfactory and the statistics for 1945–6 indicate that substantial progress has been made in reducing the death-rate.

4. There are, however, two peaks in the age mortality—at ages 5–14 and after age 55. In the youthful period the peak is more distinct for boys. The death-rate for boys under 5 in 1945–6 was still equal to that in 1920–2.

5. In each triennium of the period reviewed the female death-rate is approximately 40 per cent less than that for males, and there is suggestive evidence that the incidence of the disease is higher in males.

6. There is, as might be expected, a higher death-rate in rural than in urban areas. The occasions for this should diminish with improved hospital and transport services.

7. The mortality for males in Social Classes I and II (higher economic grades) is approximately twice that in Social Classes IV and V (lower economic grades), and this notwithstanding that the opportunities of early diagnosis and skilled surgery should be better in the higher groups. Married women in the higher economic grades also have a higher death-rate than those in the lower grades. The reasons for this differential experience are not yet apparent; they may be connected with dietary habits.

8. After careful screening, involving a close scrutiny of all case notes, 499 cases—nearly one-third—were excluded from the 1573 indexed as ' appendicitis ', leaving 1074 cases of ' proved appendicitis '.

9. The proportion of cases with peritonitis (Groups 2, 3, 4—Turner's classification) in the Radcliffe Infirmary series of 1074 cases was 48 per cent for males and 45 per cent for females; with abscess, 10 per cent for males and 9 per cent for females.

10. The case fatality in this series was 1·40 per cent, the highest case fatality—6·2 per cent—being associated with diffuse peritonitis (Group 4).

11. The fatality in the several groups was compared with that in Grey Turner's series, which covered a thirty-four-year period ending in 1934. The most striking difference between the two series was in connexion with the complication of general peritonitis (Group 4), which showed a fatality of 6·2 per cent, as compared with Grey Turner's figure of 29·2 per cent. Chemotherapy was, in all probability, chiefly responsible for the improved results.

12. Of 1027 cases in which the necessary information was included in the notes, 75·5 per cent came to operation within 48 hours of the first symptoms. While 83 per cent were in hospital within 48 hours, 25 per cent of these were already in one or other of the complicated groups (3, 4, 5, 6). Of the 175 cases treated later than 48 hours, 57 per cent were in the severe groups. In 143 cases (14 per cent) delay was greater than 72 hours, and all but 3 of the 15 fatal cases showed a delay of more than 72 hours. In 480 cases delay was less than 24 hours, but 25 of these cases already had general peritonitis; and in 164 cases the symptoms had been present for only 12 hours, but 22 cases were already in Groups 3 or 4. Delay of only a few hours may be highly dangerous.

13. In the matter of treatment the evidence strongly supported the employment of chemotherapy (sulphonamides *and* penicillin) in all cases in which inflammation has extended to the peritoneum.

14. It is concluded (*a*) that chemotherapy has largely removed the necessity for drainage, excepting in cases where oozing of blood at operation has been considerable; for chronic, thick-walled abscesses, and if closure of the appendicular stump is uncertain (cæcostomy); and (*b*) that the use of multiple drains is generally inadvisable.

15. The importance of routine bacteriological study in cases of wound sepsis is emphasized.

16. Various factors influencing wound healing are analysed and discussed. There is evidently less wound sepsis when nylon rather than catgut is used as suture material, and when drainage tubes are avoided.

We would like to record our thanks to the late Professor J. A. Ryle and to Mr. D. C. Corry for their assistance and helpful criticism; to those members of the surgical staff of the Radcliffe Infirmary whose case notes we have been privileged to peruse; to Mr. H. Cotton, Mr. L. E. Griffith, Mrs. W. F. McKay, and the staff of the Nuffield Bureau of Health and Sickness Records, for valuable assistance in the tabulation of data; and to Miss P. Coombs and the staff of the Records Department of the Radcliffe Infirmary, for the trouble taken by them in extracting the necessary case notes for study.

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DIVERTICULA OF THE APPENDIX AND CERTAIN FACTORS IN THEIR DEVELOPMENT*

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I. THE LITERATURE

A. ACQUIRED DIVERTICULA

DIVERTICULOSIS of the appendix was first described by Kelynak in 1893; he reported a "greatly distended appendix, totally shut off from the cæcum, and having two very distinct diverticular processes, which were directed between the folds of the mesentery of the appendix". Some later writers have given the credit for the first description to Edel's paper of 1894, though Edel himself refers to Kelynak's work. Edel thought diverticula were the result of distension.

'Inflammatory' and 'Non-inflammatory' Diverticula.—Soon afterwards the idea was brought forward that diverticula of the appendix were either 'inflammatory' or 'non-inflammatory', according to whether or not inflammatory damage had played a part in their development. (I have not been able to find the origin of this idea.) Hansemannn (1896) considered that non-inflammatory diverticula were due to herniation of mucosa through the openings in the muscularis by which vessels run to the inner coats. Mertens (1902) and Mundt (1903) thought that only non-inflammatory diverticula pass through these vascular openings.

Von Brunn (1905) observed that the diverticulum might contain the entire mucosa, so that the lumen of the apppendix described a sharp hairpin bend outside the muscle. He held that inflammatory diverticula may be recognized by the presence of muscle in their walls, carried out from the muscularis; Aschoff later (1908) gave this view the support of quotation. A number of other writers reported cases in the first decade of this century, discussing the findings and sometimes arriving at contradictory conclusions; for example, Maalöe (1908) supported Mertens' view that only non-inflammatory diverticula pass through the vascular openings, but Malatesta (1908) said that the vascular openings favour the development of inflammatory diverticula. Malatesta held that muscular contraction would enlarge the vascular openings and at the same time expel the mucosa.

Bérard and Vignard (1914) distinguished hernial and inflammatory types, the former being caused by rise of intra-appendicular pressure, the latter by limited necrotic lesions; these writers described morphological peculiarities of each type, but added that the former must be prone to inflammation and so to become more and more like the latter.

Lewisohn (1918), having done experimental Ramstedt operations on six dogs, found in one of them, at autopsy three months after operation, a diverticulum of the mucosa running through the defect he had made in the muscle, which in the other cases had been closed by scar tissue. He thought the diverticulum had been caused by muscular contraction soon after operation.

Chauvin (1920) reviewed the literature to date, and proposed the following classification of acquired diverticula:—

1. *Inflammatory.*—They are caused by destruction of part of the wall deep to the intact mucosa, and are of two types:—

a. Traction or cicatricial type, caused by indrawing of the intact mucosa.

b. The inflammatory focus points into the lumen, and the resulting fibrous-walled cavity becomes epithelialized.

2. *Of Intra-appendicular Hypertension.*—They are due to obliteration of the lumen and distension, are usually mesenteric, and have walls mainly fibrous.

3. *Non-inflammatory Physiological.*—These occur at the vascular openings in the muscle and are neither pulsion nor traction diverticula but "*hernies de faiblesse*". (This is difficult to understand; how can there be a hernia without pushing or pulling?)

Wilkie (1920) reported two cases of carcinoid tumour of the proximal part of the appendix with multiple mesenteric diverticula more distally. Wilkie said of the second that the diverticula "include all the coats of the appendix"; but the beautiful illustration seems to show clearly that the diverticula penetrate the muscle. He remarked that the "association of diverticula in the distal portion of the appendix with an obstructing tumour in its proximal part is self-evident in explanation".

The Function of the Muscularis (Stout).—Stout (1923) concerned himself mainly with considering what might be the force responsible for the herniation of the mucosa. He reported 4 new cases showing diversion of the entire lumen (which unknown to Stout had previously been described by von Brunn (1905), Malatesta (1908), and by Francini (1910)). But Stout drew from this phenomenon a novel conclusion: "It is inconceivable, for me at least, to imagine that the force exerted by the expansion of a fluid or a gas within the lumen of an appendix could *alone* be sufficient to force the entire circumference of the mucosa and submucosa through a defect in the muscularis". He pointed out that so far the function of the muscularis had been overlooked. He regarded the muscularis as forming with the serosa and subserosa a single coat, a tube containing the mucosa, muscularis mucosæ and submucosa; these inner coats in their turn he thought of as a single structure and "regarded as fluid". This view provided an explanation for the phenomenon of complete diversion of the lumen.

In Stout's 7 cases, all had muscular coats of greater than average thickness and vascular openings of greater than average size. His averages were based on his own measurements in 96 appendices.

* Based on a Thesis awarded the Degree of M.D. of Cambridge University.

He pointed out, however, that two of his cases had no demonstrable obstruction to the lumen; so muscular thickening is not necessarily the result of obstruction and muscular hyperactivity.

Stout also did experiments on the appendices of living dogs and on one human appendix immediately after its surgical removal. He cut gaps in the muscle coats, leaving the inner coats intact; the act of cutting the muscle stimulated it to contract; as it did so, the mucosa and submucosa were invariably herniated through the gap. If the gap were not made until after the muscularis had ceased to contract on stimulation, no diverticulum appeared unless the appendix were moderately distended artificially; but extreme distension obliterated the diverticula by their withdrawal into the increasingly rounded appendix. His conclusion was that "the chief active force in driving the mucosa and submucosa through the weak point in the muscular wall is the contraction of the circular and longitudinal muscle coats".

Stout's paper marked a definite advance over its predecessors by its originality, its clarity, and its restrained but definite conclusions.

In the next few years came almost a score of case reports and associated discussions of varying importance. The paper by Colle (1927) was useful by reason of its voluminous review of the literature. One may mention the evidence brought forward by Gardham, Choyce, and Randall (1928) and by Masson and Hamrick (1930) to show that pseudomyxoma peritonei may be caused by rupture of diverticula of the appendix. Crespellani (1927) and Kadrnka and Sarasin (1932) reported cases diagnosed radiologically. Mosinger and Imbert (1933) reported a case in which the appendix showed "marked nervous hypergenesis", and Desjardins (1933) drew attention in a similar case to the hypertrophy of the musculo-nervous complex of the submucosa. This complex had been described by Masson in 1930; he found it hypertrophied in appendices with pronounced fibrosis of chronic inflammation.

The Function of the Muscularis (Edwards).—Two most important papers on colic and appendicular diverticula were published by Edwards (1934, a, b). They were parts of the Jacksonian Prize Essay for 1932, and were to form part of his book on *Diverticulosis and Diverticulitis of the Intestine*, published in 1939. In this large-scale work, the fruit of years of study and beautifully illustrated, the author brought forward much evidence to show that diverticulosis of colon and appendix is the result of irregular or abnormal contraction of the muscularis. He considers that prolonged contraction of the longitudinal coat is probably a very important factor, for it must cause shortening of the tube and consequent folding or sacculation of the mucosa. Contraction of the circular coat would then tend to expel the mucosa through any weak point in the muscularis, usually a vascular opening, sometimes an area of inflammatory weakening.

Edwards is convinced that passive distension does not of itself cause colic diverticula, but believes it may cause at least some appendicular diverticula. He points out that distension is certainly not indispensable, for two of his cases had appendicular colic and radiologically diagnosed diverticula. He distinguishes two types of appendicular diverticula:—

1. Herniation of mucosa through a gap in the muscularis—sometimes solely by obstruction and distension.

2. Distension of mucosal sacculations, with thinning and disappearance of the muscle over them. He also distinguishes two exciting causes—passive distension and irregular muscular action; and two predisposing causes—the vascular gaps in the muscle and inflammatory gaps in the muscle.

Edwards refers to the work of Stout as pointing to the same conclusion as his own, that hernial diverticula of the intestine in general have a myogenic origin.

Galambos (1936) observed radiologically an appendix in which spastic contraction of the proximal and distal parts was accompanied by variable, transient, and recoverable sacculation in the middle part; this is strongly reminiscent of the mechanism proposed by Edwards. Collins (1936) in the same year gave a large-scale review of the literature (with several misquotations, particularly of Stout), and analytical tables of the recorded cases, and reports of 30 new cases.

Wolff (1938) reported 33 new cases, with occlusion or narrowing of the lumen in most. He considered that obstruction of the lumen leads to muscular contraction, and this to hypertrophy, whereby the intraluminal pressure is increased and the mucosa and submucosa herniated through a weak point in the muscle.

Inflammatory Destruction as a Prime Factor (Kline, Young, and Straus).—Kline, Young, and Straus (1941) presented the biggest series of cases, with 85 diverticula in 49 out of 10,000 appendices. Their study of these examples led them to conclude that acquired diverticula are formed by the growth of mucosa and submucosa into cavities formed by inflammatory destruction of the wall of the appendix. They said that muscle hardly regenerates at all, but did not mention the muscularis mucosæ. They did not give much histological detail; nor did they mention the myogenic theory, nor the theory of intraluminal pressure beyond a single quotation from Collins. If this paper had contained more evidence that the authors had given much thought to possible modes of formation of diverticula other than the inflammatory, it would have carried more weight.

Remarks on the Literature on Acquired Diverticula.—The above references comprise less than half the total contributions to the literature up to 1945. They include all the most important contributions, and have been selected to bring out certain points. First, there have been various attempts at classification, most of which are based on theories of causation. These theories in their turn are often based on isolated observations made by the classifying author or by some other worker, the observations having been related to one another in a more or less speculative way. It is, of course, an inherent weakness of the morbid anatomical method that it cannot define time relationships with anything like the same accuracy as it can define spatial relationships. It follows that classifications so founded may present

an air of clarity and completeness not necessarily justified.

The papers of Stout (1923) and Edwards (1934, a, b) are outstanding for exact observation and cautious deduction; and these authors are also the most reserved in their classifying. Even the best of the other papers cannot come up to theirs, and the majority rank far behind. And it is remarkable that only a handful of the others even mention the activity of the muscular coat of the appendix.

It appears from the literature on acquired diverticula that further consideration should be given to the following questions: (1) In the development of diverticula of the appendix, what parts are played by (*a*) Distension, (*b*) Muscular activity, (*c*) Inflammation? (2) How are these factors related?

B. CONGENITAL DIVERTICULA

Hedinger (1904) found at autopsy on a stillborn infant that the appendix bore numerous diverticula. His pictures show clearly the fundamental characteristic of congenital diverticula: that the muscularis of the appendix entirely encloses the diverticular processes of the mucosa. This report of Hedinger's had the merit not only that it was unique, but also that there could be no doubt that the diverticula were congenital.

Further cases were reported by Sisojeff (1911) and Martini (1911). Lorillou reported a case in his degree thesis of Lyons (1912–13); he had the material from a Dr. Jacquemet, of Grenoble, whose name is attached to the case in most reviews. Sturm (1915) reported 2 cases in stillborn infants with other congenital abnormalities.

A case of supposed congenital diverticula was reported by Rouffiac in 1923; but his figures contradict his claim. It seems more likely that the condition reported arose in a manner akin to that suggested by Lejars and Ménétrier in 1904, on the basis of earlier inflammatory destruction and later repair.

New congenital cases were reported by Bachlechner (1924); in 1925 there were no less than four such reports (von Faykiss; Schminke; Gullotta; and Malone). Gobbi (1927) reported a curious case of an appendix found in a hernial sac and bearing two congenital diverticula.

Walmsley (1929) and Hadley and Cogswell (1936) reported cases of intramuscular diverticula which they all regarded as Meckel's diverticula; they suggested that the vitello-intestinal duct had been attached to the gut at the point where the anlage of the cæcum was to appear. The case of Hadley and Cogswell was particularly remarkable for a cord leading from the apex of the diverticulum to the underside of the umbilicus.

Three of the 8 cases of appendicular diverticula reported by Sauer (1930) were described as "surrounded by muscle" or "having muscle in the wall", but he did not claim them as congenital or discuss the matter at all.

Kline (1935) found an example which he regarded as congenital, though he admitted it "might well be questioned". Donovan and Aguirre (1936) claimed as congenital one of their two cases; but their figure leaves no doubt that the diverticulum is 'acquired'. Two of the cases of Collins (1936) were claimed as congenital, but not illustrated. Another report came from Schläpfer (1937), and another from Altemeier (1945); from internal evidence the latter example is surely one of the 'acquired' type.

II. CASE REPORTS

In the present study there were found 19 cases of acquired or extramuscular diverticula. Their important morphological details are summarized in *Table I.* A selection are described more fully below.

(Of the intramuscular diverticula observed, only one (*Case* 25) is presented here, because its nature is not in doubt. The others might be described as curiosities of unknown origin; only one of them was perceptible macroscopically; and they do not affect the substance of this paper.)

Case 2 (*Figs.* 66, 67).—From a woman of unknown age; no history obtainable.

A large swollen appendix 7·0 cm. long, and 1·0 cm. in diameter at the distal end; lumen greatly reduced.

In the sections may be seen submucous fibrosis and considerable muscular hypertrophy. Although the mucosa in its normal situation shows no sign of acute inflammation, there is general acute inflammation of the serosa, which has spread from the apex of the mesenteric diverticulum, where its mucosa is destroyed by acute inflammation. The diverticulum passes through a vascular opening and has a muscularis mucosæ.

Case 3 (*Fig.* 68).—From a married woman; age, history, etc., are not known.

An appendix 7·0 cm. long, 1·0 cm. in diameter. Some congestion of the serosa.

The main features observed microscopically are: A mesenteric diverticulum, having good mucosa and muscularis mucosæ, passes through a vascular opening; there is slight inflammation. The muscle of the appendix is thick, the submucosa fibrotic.

Case 8 (*Figs.* 69–71).—From a woman with a history of 'subacute appendicitis' for two years—recurring attacks of pain in the right iliac fossa, with vomiting.

The appendix is 7·0 cm. long, and angled through 90° 2·0 cm. from its proximal end. The proximal part is of normal external diameter, but the distal part is considerably dilated, and filled with clear mucoid fluid. The appendix has been cut longitudinally, and one-half again cut transversely through two diverticula, one of 1·5 cm. diameter, the other of 0·7 cm. A third lateral diverticulum is to be seen, and also a fourth near the tip (*Fig.* 69).

A longitudinal section of the distal part shows two diverticula; one of the proximal part shows the dilated cavity lined by fibrous tissue, and also the narrowing of the lumen in the most proximal region. There is no definite evidence in either section that any diverticulum passes through a vascular opening. The muscle must surely be considered hypertrophic, if it be remembered that it must have been stretched and thinned by the distension.

Case 9 (*Fig.* 72).—A man aged 47. History of pain in the right iliac fossa; classical signs of acute appendicitis.

A zig-zag appendix, 7·0 cm. long, with fibrin and congestion confined to the surface, the inner parts being fibrotic and pale. A suspected diverticulum seen with the naked eye.

The section shows a diverticulum passing through a vascular opening of doubtful position, and having a

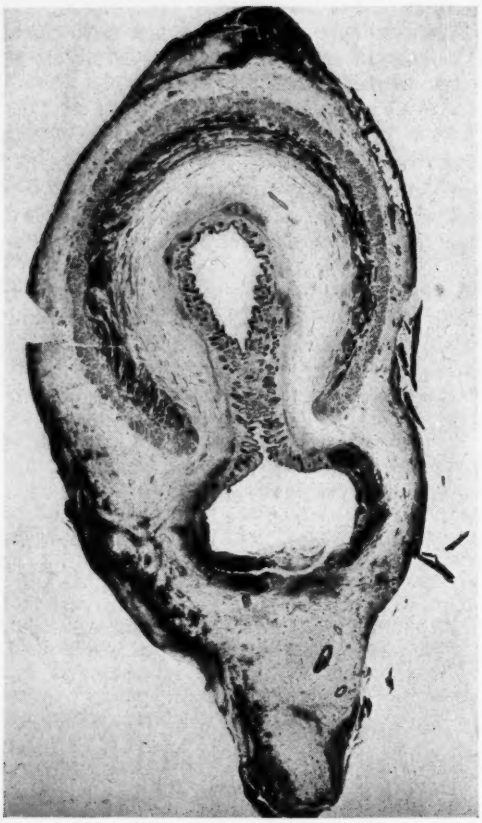

FIG. 66.—*Case* 2. A section running almost exactly through the aditus of the diverticulum. Note the hypertrophy of the muscle and the submucous fibrosis. The mucosa is not wrinkled. H. and E. (× 4·5.)

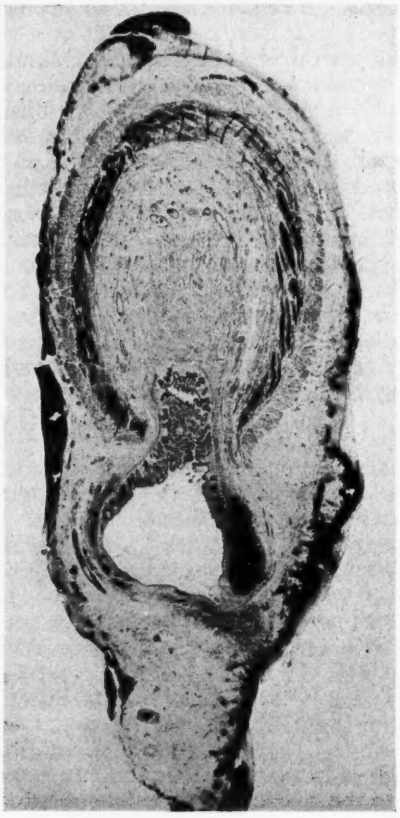

FIG. 67.—*Case* 2. Another section showing the track of the inflammation from the diverticulum to the serosa. Also seen are the muscularis mucosæ of the diverticulum, and the vessels in the opening in the muscle—on the right. H. and E. (× 4·5.)

FIG. 68.—*Case* 3. A mesenteric diverticulum, with good mucosa and muscularis mucosæ, passes through a vascular opening. Note the submucous fibrosis and thick muscle. H. and E. (× 4·5.)

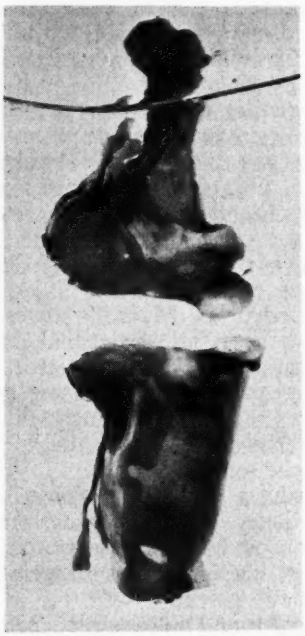

FIG. 69.—*Case* 8. The bottled specimen, being one half of the appendix after longitudinal section; a transverse cut has also been made through two diverticula, one on either side. A third is on the left, in the distal (lower) portion, and a fourth at the apex. The angulation of the appendix can be made out just above the two diverticula at the transverse cut. (× 0·8.)

muscularis mucosæ. The muscularis of the appendix is hypertrophic, the submucosa fibrotic.

It can also be seen that the mucosa of the diverticulum has opened out around its ruptured apex in a mushroom-like fashion. This, and similar things seen in other

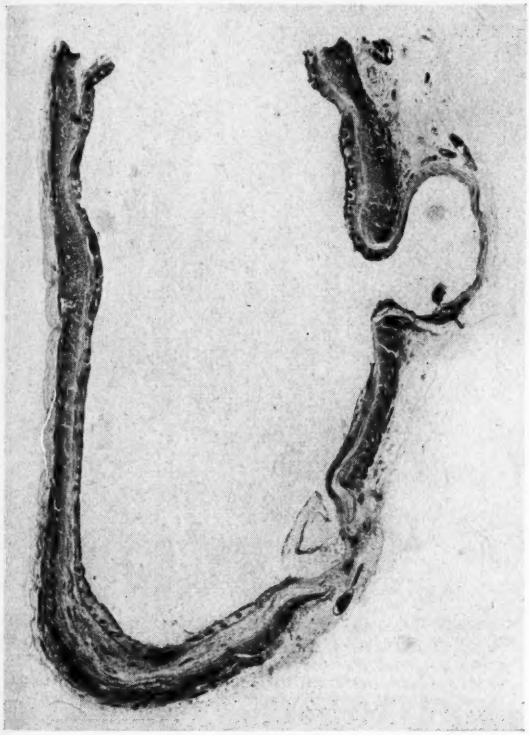

FIG. 70.—*Case* 8. Longitudinal section of the distal part of the appendix. The diverticulum nearer the upper end corresponds to that seen in *Fig.* 69 on the left (the 'third'). H. and E. (× 5.)

examples, are surely like in nature to the eversion of mucosa which occurs when the intestinal tract is opened

FIG. 72.—*Case* 9. Notice particularly the curious mushroom-like fashion in which the mucosa of the diverticulum has opened out around its ruptured apex. H. and E. (× 4·5.)

at operation—an eversion, as Stout put it, "familiar to all who have seen it". Observations such as this may have a bearing on the theory advanced by Gardham and others (1928) on the development of pseudo-myxoma peritonei.

Case 16 (*Figs.* 73–77).—A man of 40 had seven days' umbilical pain, moving into the right iliac fossa; in this situation there was rigidity and a 'doubtful' mass. At operation a mass was in fact found, and some pus;

FIG. 71.—*Case* 8. Longitudinal section of the proximal part, showing loss of mucosa except in the constricted basal portion. H. v. G. (× 5.)

the appendix was removed, with some difficulty, "perforated in several places".

The appendix as received in the laboratory after fixation was a remarkable sight. It was 13·0 cm. long, and was thrice bent at about 90°, and thus divided into four nearly equal parts. The three proximal parts lay in one plane, but the terminal quarter was in a plane

FIG. 73.—*Case* 16. Sections from a series cut from the region of the junction of the third and fourth parts of the appendix, showing the considerable diminution of the lumen. H. and E. (× 4·5.)

perpendicular to that. The lumen was small in the second and third quarters, and very small at the junction of the third and fourth quarters. In the fourth quarter

a number of diverticula were found. One was a pale rounded projection 4·0 mm. in diameter, rising from the mesenteric fat 3·0 cm. from the tip of the appendix. Another, 4·0 mm. in diameter, surrounded by a red zone, lay on the antimesenteric border 1·5 cm. from the tip. The tip itself had a bulbous prolongation 7·0 mm. overall. And a fourth diverticulum was found on the mesenteric border when a transverse knife-cut was made 3·5 cm. from the tip of the appendix.

The sections showed widespread acute inflammation, submucous fibrosis, and muscular thickening (though the muscle had been stripped off parts of the first and third quarters during the operation). Vessels were not found at the neck of the antimesenteric diverticulum, though they were in the other three diverticula; and all the four examples had muscularis mucosæ. A short series of sections taken at the narrowest part of the lumen failed to show complete obliteration.

FIG. 74.—*Case* 16. This mesenteric diverticulum was 3·5 cm. from the tip of the appendix. The vessel running through the opening can be seen on the left; the muscularis mucosæ is well shown. Note the mucosal folding. H. and E. (× 4·5.)

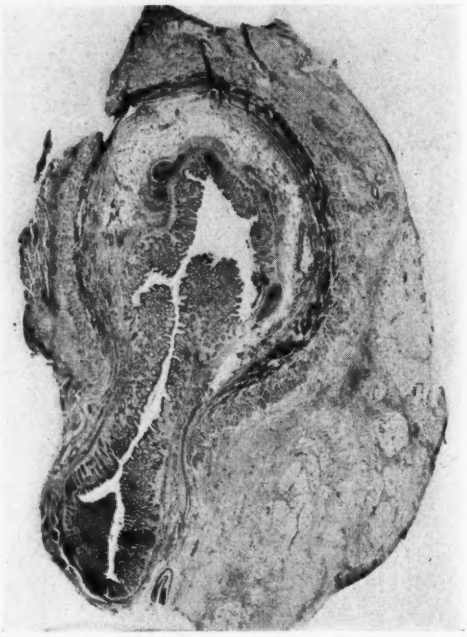

FIG. 75.—*Case* 16. This mesenteric diverticulum was 3·0 cm. from the tip of the appendix. Its muscularis mucosæ is well seen, as also the curved longitudinal section of the artery running out from the right of the vascular opening. There is much mucosal rugosity. H. and E. (× 4·5.)

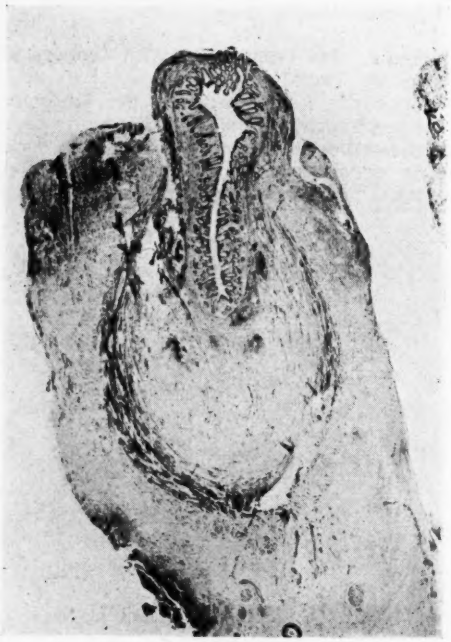

FIG. 76.—*Case* 16. A section of the antimesenteric diverticulum 1·5 cm. from the tip of the appendix. H. and E. (× 4·5.)

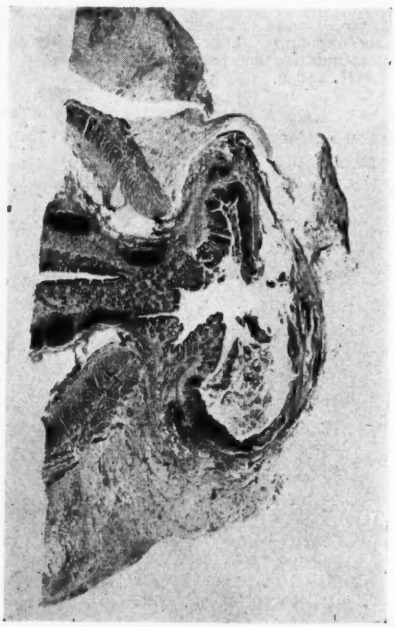

FIG. 77.—*Case* 16. A section of the apical diverticulum, rather damaged, presumably in the theatre. It had muscularis mucosæ all around its proximal half. H. and E. (× 4·5.)

Figs. 73–77 show the zone of stenosis and the four diverticula, in order of progression towards the tip of the appendix.

Case 17 (*Figs.* 78, 79).—Found at post-mortem on a man who had collapsed on a bus and died almost immediately from a coronary thrombosis. There were many pericæcal adhesions.

FIG. 78.—*Case* 17. This is a section of the flattened region, in which the normal mucosa has quite been replaced by fibrous tissue. H. and E. (× 4·5.)

The appendix was 8·0 cm. long, with a free opening into the cæcum. The diameter of the proximal 5·5 cm. of its length was about 0·7 cm.; then came a zone in which it was flattened from side to side, where it measured 1·0 cm. in the plane of the mesentery. A diverticulum 0·6 cm. in diameter lay in the mesentery immediately proximal to the apex; it was filled with clear mucus.

The sections show that in the flattened region all traces of the mucosa and lymphoid tissue have been replaced by fibrous tissue. Distal to that there is a lumen lined by a single layer of columnar epithelium, and slightly distended; the muscularis is very thick and is infiltrated by fine fibrosis. The diverticulum runs through the apical vascular opening, and has no epithelial lining; it is lined in some parts by foreign-body giant-cells and macrophages, but elsewhere the lining is fibrous. Mucus secretion and accumulation were demonstrated by Masson's trichrome stain.

Clearly an attack of inflammation has destroyed the lumen at the flattened part and most of the mucosa distal to it, but left enough mucosal cells to regenerate and cover the sequestrated part of the lumen. The mode of formation of the diverticulum is further discussed later.

Case 19 (*Figs.* 80–84).—From a woman of 26. She had a baby in March, 1946. About a week after delivery she first noticed pain in the right iliac fossa. The pain was not colicky at this or any other time; it was inconstant for a few weeks. At the end of May, 1946, she had umbilical pain which moved to the right iliac fossa; there was vomiting, walking was painful, and she went to bed. On June 11 there was a tender ill-defined mass in the right iliac fossa; at laparotomy an appendix abscess was found and drained without appendicectomy. The cæcum and the pericæcal adhesions were described as "very hard and thick". Early in February, 1947, she had a sudden pain in the right iliac fossa on rising from a chair, and was left with a nagging pain, worse on carrying anything. Appendicectomy was done on March 20, 1947.

FIG. 79.—*Case* 17. On the left is the fibrous bulkhead obliterating the lumen, then the slightly expanded lumen lined by a single layer of secreting epithelium and surrounded by thick muscle. The tip of the appendix is curved over, and through the apical opening the cavity communicates with the mucus-filled diverticulum. H. and E. (× 4·5.)

The appendix was rather long but quite slender. There was a very obvious bulge on the mesenteric border just proximal to the apex, rather more than hemispherical and about 1·0 cm. in diameter. This was a diverticulum with a mucosal outline roughly D-shaped. Elsewhere the lumen of the appendix was very narrow.

The sections show that the diverticulum passes through a vascular opening, has fairly normal mucosa,

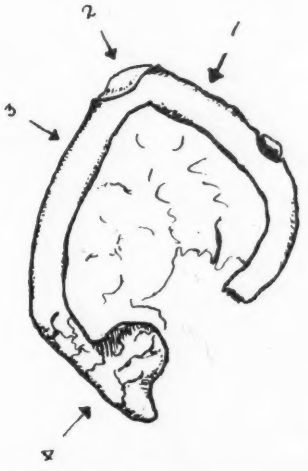

FIG. 80.—*Case* 19. (Also Experiment 6). A sketch of the appendix, showing the mesenteric diverticulum close to the tip, and two experimental diverticula on the antimesenteric border. The arrows show the planes of *Figs.* 81–84 in numerical order. (× 1.)

muscularis mucosæ, and some other muscle-fibres in its wall. There was no muscular thickening at any part. Total fibrous obliteration of the lumen was found at a point 5·5 cm. from the apex of the appendix, but there

was no suggestion of distension at any point in the distance between here and the diverticulum. That mucus was being formed was shown by Masson's trichrome staining of sections at two points in between, though the mucosa is poor and mucus secretion not general. By comparison there is more mucus formation in the mucosa of the diverticulum.

Case 23 (*Figs.* 85, 86).—A woman of 23 had two days of epigastric pain, which shifted to the right iliac fossa; typical signs of acute appendicitis were present.

The appendix was 5·5 cm. long, with a large mass of mesenteric fat. It was generally suffused on the exterior, with some granular and flaky fibrin. On cross-section there was no internal congestion.

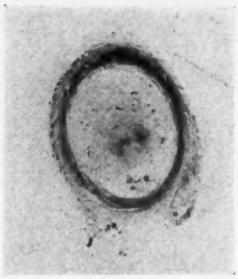

Fig. 81.

Fig. 82.

Fig. 83.

FIG. 81.—*Case* 19. This cross-section (at 1, *Fig.* 80) shows the complete loss of mucosa and replacement by fibrosis. H. and E. (× 4·5.)

FIG. 82.—*Case* 19. Showing the size of the lumen (at 2, *Fig.* 80); it was nowhere larger than this, and mostly smaller. This figure also shows how the muscularis is breached in making an experimental diverticulum. H. and E. (× 4·5.)

FIG. 83.—*Case* 19. A cross-section showing the small lumen, with scanty mucosa (at 3, *Fig.* 80). H. and E. (× 4·5.)

The sketch (*Fig.* 80) shows by numbered arrows the planes of the succeeding photomicrographs, which appear in the same order. Also seen are two experimental diverticula, of which more will be said later; they are on the antimesenteric border.

Fig. 84.

FIG. 84.—*Case* 19. The diverticulum; the mesenteric border is at the bottom. In the section the muscularis mucosæ can be seen almost completely encircling the diverticulum. The vessels at its neck on the right are seen in the photograph, and some isolated muscle-bundles, not muscularis mucosæ, on the left.

FIG. 85.—*Case* 23. Showing the abscess associated with the more proximal diverticulum, and the path of the inflammation to the serous surface of the meso-appendix. There was only minimal inflammation of the main lumen. H. and E. (× 4·5.)

FIG. 86.—*Case* 23. The more distal diverticulum, in continuity with the main lumen. Note the remarkable prolongation of the muscularis far out into the mesentery, from the right margin of the vascular opening. H. and E. (× 4·5.)

Two diverticula were found on the mesenteric border in the distal half of the appendix. Each passes through a vascular opening in the hypertrophic muscularis, each has muscularis mucosæ. As the figure shows, an abscess has developed near the apex of the more proximal diverticulum and has pointed on to the surface of the mesentery, whence the wide serosal inflammation has spread. In the other figure, of the more distal diverticulum, may be seen a remarkable prolongation of the muscularis into the mesentery.

Case 24 (*Figs.* 87–89).—A woman of 38 had continuous and increasingly severe pain for 48 hours, with some vomiting, and with tenderness in the right iliac fossa and on rectal examination.

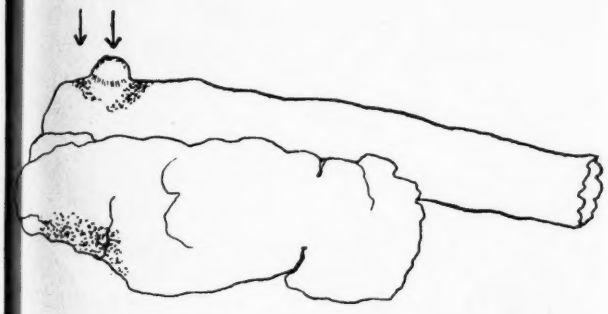

FIG. 87.—*Case* 24. A sketch showing the dome-like projection on the antimesenteric border near the tip; the stippling around its base indicates the distribution of fibrin, which was also present on the mesenteric fat opposite.

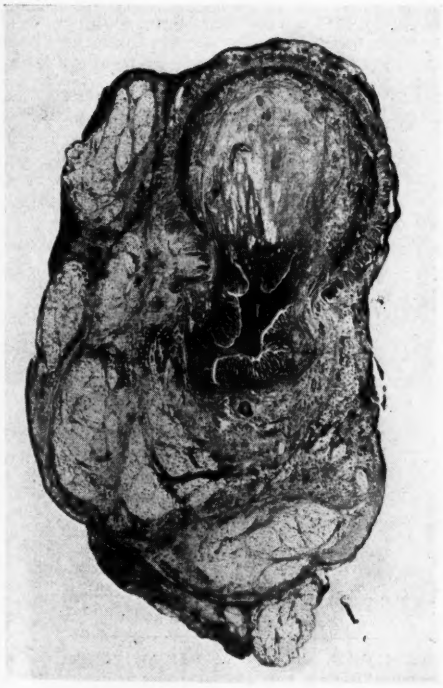

FIG. 88.—*Case* 24. This section was made from the more proximal of two blocks made after a transverse cut at the more distal arrow in *Fig.* 87. The mucosal structures lie almost completely outside the line of the muscle, having gone through a vascular opening. H. and E. (× 4·5.)

The appendix was 7·0 cm. long, with external diameter of 1·0 cm., though slightly thicker in the distal quarter. The lumen seemed small throughout. On the antimesenteric border about 1·0 cm. from the tip was a small, red, hemispherical projection of the serous surface, which bore also granules of fibrin around the base of the projection. A transverse cut 0·5 cm. from the apex of the appendix revealed an inflamed zone in the mesentery just outside an opening in the muscularis.

Microscopically it was found that the antimesenteric bulge was an abscess, lying just outside a vascular opening in the muscularis; but there was no evidence that it was connected with the lumen proper of the appendix. The more distal mesenteric inflamed zone was found to be a diverticulum; this example is peculiar in that apparently the tip of the mucosal tube has been completely diverted from the muscular tube through a vascular opening in the mesenteric border.

A section from the middle of the appendix, where the lumen was most severely constricted, confirmed the naked-eye observation.

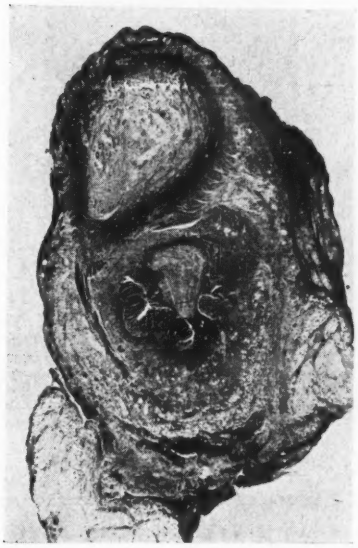

FIG. 89.—*Case* 24. The more distal part from the region of the more distal arrow in *Fig.* 87. The mucosa lies in the mesentery quite outside the muscular ring, which here is closed. Observe the 'tail' of muscle running down into the left of the mucosa. H. and E. (× 4·5.)

A Case of Congenital Diverticulosis.—This example was found at post-mortem in The Hospital for Sick Children, Great Ormond Street. I am indebted to the Medical Committee of that hospital for permission to publish the case.

Case 25 (*Figs.* 90, 91).—A female infant died at the age of five weeks. The following abnormalities were found: patent ductus arteriosus, patent interventricular septum, cleft palate, hare-lip, fusion of right and left frontal lobes of the brain, and deficiency of the bones of the cranial vault.

The photograph of the appendix shows that there were at least three roughly conical projections of its surface. Microscopy shows that these are diverticula in the walls of which are the normal structures of the wall of the appendix. The muscularis in particular is continued over their convexities without interruption and with only the slightest thinning. These are undoubtedly congenital diverticula.

III. EXPERIMENTAL WORK

General.—A few experiments were carried out on the lines of those of Stout (1923). At first I tried to make openings in the muscle by the use of an

iridectomy trephine, with the object of controlling the size of the openings; but it was unexpectedly difficult to be sure how deep the trephine was going, and, moreover, I never succeeded in making in this way an opening through which an artificial diverticulum shortly afterwards appeared.

All the experiments now to be described were performed on human appendices immediately after their surgical removal. The appendices showed little or no acute inflammation, most none at all. The procedure was this: Immediately the appendix was cut off from its cæcal end it was dropped into normal saline at 100° F. (the appendix cools quite noticeably even in the short time that passes before

FIG. 90.—*Case* 25. The appendix of the five weeks' old infant with other congenital abnormalities. Three conical projections are seen on its convex border. (× 1.)

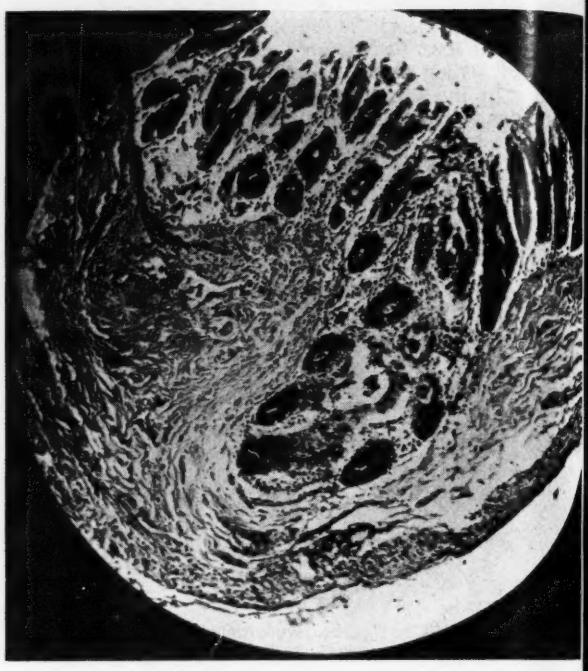

FIG. 91.—*Case* 25. From a section running through one of the conical projections seen in *Fig.* 90. The muscle runs from side to side of the lower part of the figure, enclosing the diverticular process of mucosa, and not being itself thinned. There is a very clear contrast with the arrangement seen in most of the other cases in this series. (× 60.)

Table I.—IMPORTANT MORPHOLOGICAL DETAILS IN APPENDICES WITH EXTRAMUSCULAR DIVERTICULA

	Extramuscular Diverticula													
	Via Vascular Opening				*Via Other Openings*									
Case Number	Mesenteric	Anti-mesenteric	Apical	Other	Mesenteric	Anti-mesenteric	Apical	Other	*Total Number of Diverticula*	*Total via Vascular Opening*	*Total via Other Openings*	*Total with Muscularis Mucosæ*	*Muscular Hypertrophy*	*Submucous Fibrosis*
1		1m			1m				2	1	1	2	yes	yes
2	1m								1	1		1	yes	yes
3	1m								1	1		1	yes	yes
4				1m					1	1		1	yes	yes
5	1m								1	1		1	yes	yes
6	1m								1	1		1	yes	yes
8					1		1	2	4		4	?	yes	yes
9				1m					1	1		1	yes	yes
10		1m			1m				2	1	1	2	yes	yes
11	not microscoped								(3)	not microscoped				
13					1m				1		1	1	yes	yes
16	2mm		1m			1m			4	3	1	4	yes	yes
17			1						1	1		0	yes	yes
18			1						1	1		1	yes	yes
19	1m								1	1		1	no	yes
21	1m				1m				2	1	1	2	yes	yes
22				1m					1	1		1	yes	yes
23	2mm								2	2		2	yes	yes
24	1m								1	1		1	yes	yes
Totals	11	2	3	3	5	1	1	2	28 (31)	19	9	23		

m = Muscularis mucosæ present in diverticulum.

this stage is reached). After a minute or two in this bath various manipulations were performed, shortly to be described, sometimes interrupted by further periods of immersion in the warm bath. When the experiment was finished, the appendix was fixed in formol-saline.

Experiment 1 (*Fig.* 92).—This was the first to produce an artificial diverticulum in the manner of Stout (following several unsuccessful attempts). An opening 2–3 mm. in diameter was cut in the muscularis, using pointed scissors

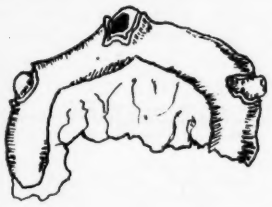

FIG. 92.—*Experiment* 1. Three artificial diverticula are seen on the antimesenteric border. In that about the middle of the length of the appendix the lumen has been entered. (× 1.)

and fine dissecting forceps. Almost at once the appendix began to shorten, and it became firmer, and a bulge appeared at the opening in the muscle. (It was near the antimesenteric border, near the tip).

Then, as I was not certain that I had dissected off either all the thickness of the muscle or only the muscle, I repeated the performance at about the middle of the appendix. Removal of what I thought to be the muscle revealed here (as before) a fibrous sheet; when I went through this I found a soft creamy tissue, and on going deeper through this entered the lumen.

The first manœuvre was then repeated as exactly as possible near the base of the appendix. There was a further contraction and another diverticulum appeared.

Experiment 2 (*Fig.* 93).—This was a long appendix *in vivo*. It underwent striking shortening on having two openings of 4–5 mm. diameter cut in its muscularis, at which openings two large diverticula appeared.

Then, a cannula having been tied into its proximal end, the appendix was distended with normal saline from a syringe. The appendix increased in length by about 3·0 cm., and the diverticula became slightly more prominent. The pressure was increased until a small

FIG. 93.—*Experiment* 2. Showing two large experimental diverticula. The appendix has been distended and ligated at its proximal end; but the size of the diverticula has hardly been increased by the distension. (× 1.)

puncture appeared in the proximal diverticulum, but there was no further increase in the size of either. The appendix was removed from the cannula (the ligature being simultaneously drawn tight) and dropped into formal-saline. Microscopical section later confirmed the breaching of the muscularis.

Experiment 3.—After this appendix was received from the surgeon it was put into warm saline as usual, but nothing further was done to it for about twenty minutes, while the surgeon finished the operation, as he wanted to see the "work". During the waiting period the appendix spontaneously shortened by about 3 cm. Three openings were made in the antimesenteric border, moving from apex to base, but there was never a suggestion of further contraction. No bulging was noticed at any opening, except that after fixation a very slight convexity appeared at the most proximal. Sections later confirmed that the muscle had been breached in two of the three openings.

Experiment 4 (*Fig.* 94).—In this case the making of two openings was followed in each case by the appearance of a diverticulum. The element of shortening in the contraction was emphasized by the extrusion of a cylinder

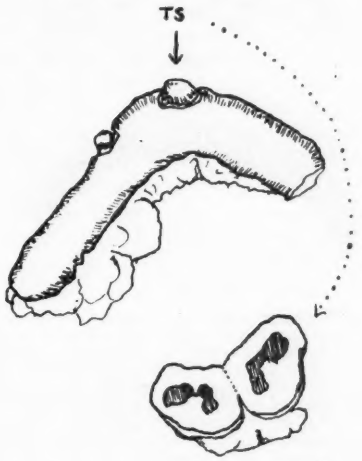

FIG. 94.—*Experiment* 4. The upper sketch shows the appendix with two experimental diverticula. One of them was cut transversely as indicated, the appearance of the apposed faces being shown in the lower drawing. Here the lumen is shaded; its angulation is pronounced. (× 1.)

of fæcal matter about 2·0 cm. long, roughly the amount by which the appendix had been shortened. It looked very much as if the rod of fæces were being pushed out by pressure on its end by the apex of the appendix. There was no visible peristaltic ring. On making transverse knife cuts into this appendix after fixation, it was found to contain solid fæces at the level of the more proximal diverticulum, and here the lumen had been quite sharply angulated.

Experiment 5.—This appendix was removed under spinal anæsthesia, and was observed to contract during handling by the surgeon, before being clamped. When it was clamped (by the particularly powerful crushing-clamp used by the individual surgeon) it gradually became considerably longer; and it could not be made to contract again, even by adding pitocin to the saline bath. It remained flaccid and inert at all times. There was no result on cutting openings in the muscularis. Inflation with syringe and cannula caused no bulging at the openings. The appendix was fixed in distension as in *Experiment* 2. Later it was cut longitudinally; everywhere the lumen lay wide open.

Experiment 6 (*See Fig.* 80).—In this case 3·0 mm. openings were cut in the antimesenteric border at the distal ends of the first and second quarters of the length of the appendix. There was no contraction, and no diverticula appeared. On adding some hot saline to the vessel containing the appendix, making the final temperature 120° F., there was a moderate contraction and small bulges at the openings. When the appendix was now removed from the saline (because somebody wanted to look at it) it relaxed and the bulges disappeared; on return to saline the appendix contracted and the bulges reappeared.

Experiment 7.—The usual procedure of cutting openings was followed immediately by diverticulum formation and shortening of the appendix to about 8·0 cm. The

appendix was then stretched in the hands to over 12·0 cm.; the diverticulum became smaller but did not completely disappear. On return to saline the appendix contracted down to 8·0 cm. again, and the diverticulum was fully restored.

Experiment 8 (*Fig.* 95).—The appendix having been moderately distended through a cannula, and a ligature tightened around its middle, the cannula was removed.

FIG. 95.—*Experiment* 8. The upper drawing shows the undistended proximal part with an experimental diverticulum on its antimesenteric border. It is an approximately mid-plane longitudinal section; note the narrow tortuous lumen angulated like an inverted U, opposite the diverticulum. The lower drawing is of the distended distal part with a slightly bulging experimental diverticulum; the cavity is wide, the mucosa is smooth. Note that the overall thickness is hardly increased by distension. (× 1.)

An opening was then cut in the muscle of the distended distal part, and a slight bulge appeared there. Next an opening was cut in the undistended proximal part, and a diverticulum appeared there. The appendix was fixed with the ligture in position. (The distension of the distal part was not so great as to make it really tense.) After fixation it was cut transversely at the ligature, and then each portion was cut longitudinally in the plane of the mesentery.

In the distal part the lumen is well open in all its length. The mucosa shows only very slight irregularities of surface; it looks as if it were firmly stuck down to the submucosa, and that in turn to the muscle. The bulge at the artificial opening, seen from inside, is a smaller than hemispherical recess of the lumen, with a wall slightly more translucent than that of other parts. The boundary between the mucosa lining this diverticulum and that around it is smoothly and gently curved.

In the proximal part the lumen is more potential than real; from it arise narrow recesses at irregular intervals. At the level of the diverticulum the lumen is sharply deviated, making a sort of U. The mucosa is much thicker than in the distal part.

The internal diameter of the muscular tube in the proximal part was at maximum 8·0 mm.; but that in the inflated distal part was actually less, being 7·0 mm.

Experiment 9.—This was essentially a repetition of *Experiment* 8, with the single but important difference that the distension of the distal part was in this case enough to make the wall of the appendix really tense. Two openings were cut in this part; at the first no bulging was seen, at the second there was just perceptible bulging. On longitudinal section (as in *Experiment* 8) there was no sign of a recess at either opening in the distal part; the wall was very thin—about 1·0 mm. or less throughout. The internal diameter of the muscular tube in both parts was 5·0–6·0 mm.

Experiment 10 (*Figs.* 96–98).—The distal half of this appendix was stretched longitudinally in an improvised extension apparatus. Then openings were made in the distal and proximal parts, in that order. There was a

FIG. 96.—*Experiment* 10. The proximal unstretched part, with experimental diverticulum and rugose mucosa. (The apical end, to the right, was clamped in the extension apparatus.) (× 1.)

FIG. 97.—*Experiment* 10. The distal stretched part. The mucosa is comparatively smooth; the experimental diverticulum is not seen. (Again the apical end is to the right.) (× 1.)

just perceptible bulge at the opening in the distal part; at that in the proximal part there was a smallish bulge, so a second opening was made, and a big diverticulum appeared. The appendix was fixed while still held in the apparatus, and then was cut across at the junction of the proximal and distal parts; each part was then cut longitudinally. In the distal part the mucosa was comparatively smooth, almost free from rugosity; in the proximal part there was pronounced rugosity.

The importance of the element of shortening, that is, of the function of the outer longitudinal muscle layer, is emphasized by *Fig.* 98. It is a longitudinal section of the proximal end of the appendix, and shows a pouting

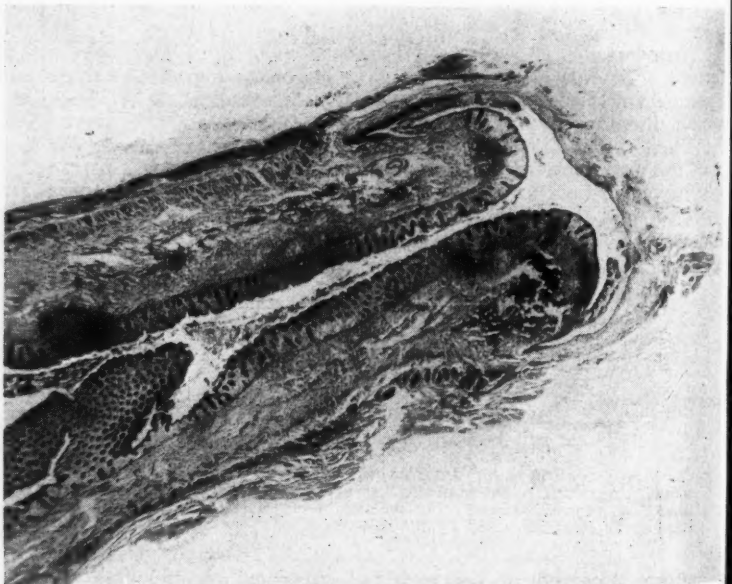

FIG. 98.—*Experiment* 10. A longitudinal section from the other half of the proximal part shown in *Fig.* 96. The different coats of the wall of the appendix, having been 'welded' by the surgeon's clamp, have acted as a fixed point, causing pouting of the mucosa and submucosa when the appendix contracted and shortened. H. and E. (× 10.)

of the submucosa and mucosa from the open end. The extreme ends of the appendicular coats, where they were cut across, do not take part in this pouting; for at that part the clamp had been applied (as can indeed be seen), and the "welding" of the coats thereby produced had

stopped the normal excursion of one coat over another. At the same time the " welding " had provided a fixed point past which the more distal mucosa and submucosa, impelled by the contraction induced by the cutting of an opening, had pouted or ' intussuscepted '.

Summary of Results of Experiments.—

1. Whenever the cutting of an opening in the muscle was followed by the appearance of a diverticulum, there was also a synchronous contraction of the muscularis of the appendix.

2. Whenever the cutting of an opening was not followed by a contraction of the muscularis, no diverticulum appeared.

3. The most noticeable feature of muscular contraction was shortening of the appendix as a whole.

4. Whenever an appendix was distended lengthening was much more striking than thickening.

5. Distension did not produce diverticula in appendices in which openings were cut in the muscularis before or after the distension.

Table II.—Experimental Work and Results

Experiment	
1.	Openings made — contraction observed — diverticula formed
2.	Openings—contraction—diverticula, scarcely enlarged by distension
3.	Contraction before openings—no further contraction—no diverticula
4.	Openings—contraction—diverticula
5.	Relaxation after clamp—openings—no contraction—no diverticula—no bulging on distension
6.	Openings—no contraction—no diverticula—hotter bath — contraction — diverticula — cooling — relaxation — diverticula disappear—heat—diverticula reappear
7.	Opening — contraction — diverticulum — stretching — diverticula reduced in size — release — contraction — diverticula fully restored
8.	Moderate distension of distal part—opening—small diverticulum ; opening in proximal part — contraction — diverticulum
9.	Strong distension of distal part—opening—no diverticulum ; opening in proximal part—contraction—diverticulum 8, 9. Internal diameter of muscular tube not greater in distended parts than in undistended parts
10.	Stretching of distal part—opening—very small diverticulum ; openings in proximal part—contraction—diverticula 8, 9, 10. Mucosa smooth in distended or stretched parts, rugose in undistended or unstretched parts

IV. DISCUSSION

INTRODUCTORY

In the literature on this subject, attention centres mainly around certain factors thought to play important parts in the development of acquired appendicular diverticula, as follows: (1) Increase of intra-appendicular pressure by distension; (2) Constrictions of the lumen held responsible for the distension; (3) Muscular activity; (4) Inflammation.

The operation of these factors was postulated in the main on the basis of observations of normal and morbid anatomy and histology. Classifications of various types of diverticula of the appendix were drawn up on a basis of the supposed predominance of one or other factor. These factors can now be re-examined in the light of the cases and experiments reported above.

1. DISTENSION

Distension not the Principal Factor in Diverticulum Formation.—Towards the end of the last century much study was given to the problem of the origin of colic diverticula. Stout (1923) quotes the experiments of Heschl (1880), Good (1894), Hansemann (1896), Hanau (1896), and Grassberger (1897), who sought to demonstrate points of weakness in the colic wall by distending human and animal colons with water, in some cases to the point of bursting; these unnatural experiments were later invalidated by the work of Chlumsky (1899) and Beer (1904). In the meantime, however, Edel (1894) and Hansemann (1896) had naturally enough applied the idea to appendicular diverticula, without direct experiment on the appendix. And this ' passive distension ' theory has continued to exercise an influence almost to the exclusion of anything else, the work of Stout and Edwards notwithstanding.

The general conclusion of these two workers, that distension is by no means the pre-eminent factor in diverticulum formation, is supported by the results of *Experiments* 2, 5, 8, and 9, reported above. Of course, the distending force used in this sort of experiment is applied much more rapidly, and may well be much greater, than would be the case in natural disease. Moreover, under natural conditions there would be time and opportunity not only for greater stretching of tissues, but also for their rearrangement, and for the formation of new tissue to allow for expansion.

None the less it seems reasonable to conclude that passive distension of the appendix cannot by itself be the cause of the common morphological forms of extramuscular diverticula.

2. STENOSIS OF THE LUMEN

Stenosis not always present.—The literature contains many statements on this mechanism. Some writers emphasize it strongly; most accept it as a contributory factor of some importance. Yet in some cases no stenosis has been found; among these, the examples seen by radiography are very convincing. (In surgically removed appendices there is always the possibility that a stenosed part may be crushed by the surgeon's clamp, or left attached to the cæcum.)

Complete Obliteration of Lumen requires proof by Microscopy.—In the hope of making some observations relevant to the problem of stenosis, I examined all the surgically-removed appendices received in the laboratory in the course of a year; they totalled 207. They were all fixed in formal-saline. The method used was to make transverse knife-cuts at intervals of up to 3 mm.—usually about 2 mm., sometimes 1 mm. or less.

The intention was to discover regions of specially severe stenosis and to observe the condition of the lumen in more distal parts. In particular I hoped to find regions (other than the blind end of the appendix) showing complete fibrous obliteration of the lumen. Nearly all the slices thought macroscopically to show this state of things were embedded and cut for microscopy. In every case a lumen was found, lined

by mucosa in all but one, in which it had apparently been destroyed by acute inflammation.

The conclusion is that microscopical examination is essential to establish total obliteration of the lumen.

Estimating the Degree of Stenosis requires Measurements of Internal Circumference.—In the preparations just mentioned the outlines of the lumen in cross-section were such that it was inaccurate merely to measure the apparent diameter of the lumen. The true capacity of the lumen could only be judged on a measurement of internal circumference. Such measurements were made, using an eyepiece micrometer; the findings are shown in *Table III*.

Table III.—Microscopic Findings in Slices of Appendix thought macroscopically to show Total Fibrous Obliteration

Appendix No.	*Internal Circumference*	*Remarks: Outlines of Lumen*
	mm.	
22	2·0	A slit
50	1·5	Circular
51	2·9	Y-shaped, with long 'stem' and short 'branches'
52	6·0	Circular, filled by mucosal fold
60	5·0	Crescentic (diverticulum *Case* 14)
80	6·0	Roughly circular
108	2·0	A slit
130	0·7	Circular
131	6·0	Triradiate
162	1·5	Comma-shaped with minute tail; filled by oxyuris
180	4·5	Slit with small V at each end
190	?	Acute inflammatory destruction
216	2·0	Triradiate
220	2·7	A slit

What Degree of Stenosis is necessary to produce Obstruction?—Other measurements of internal luminal circumference were made in addition to the above—in all, 126 measurements on sections from 45 appendices. The findings were then studied to try to discover a critical value, readings below which would always be accompanied by larger readings in more distal parts of the appendix; in other words, to define a true obstructive stenosis.

If certain cases were excluded, such a threshold could be set at an internal circumference of 4·0 mm. But in one case (No. 130) the lumen proximally measured 0·85 mm., and distally only 3·5 mm.; in another (No. 151) the proximal measurement was 3·2 mm., the distal 4·0 mm. And the problem appeared still more confusing when it was discovered that in two cases there was total fibrous obliteration of the lumen which had been no more than suspected on naked-eye inspection (No. 203 and No. 217, respectively diverticulum *Cases* 17 and 19). Furthermore, in the first of these two there was distension distal to the obstruction, in the second there was not; although mucus was being formed behind the obstruction in both.

Obstructive Stenosis in Cases with Diverticula.—One thing does emerge clearly from these measurements; in every case of diverticulosis save one in which such measurements have been made, the circumference of the lumen in some part proximal to the diverticula has been less than 4·0 mm. (*See Table IV*).

Table IV.—Internal Circumferences in Appendices with Diverticula

Case No.	*Proximal to Diverticula*	*In Planes of Diverticula*
	mm.	mm.
1	1·0	—
2	7·3	23
3	—	27
6	3·0	—
8	—	Up to or over 50
16	3·5	9–10, 13–14, and 29
17	zero	—
18	2·0	—
19	zero	20
21	2·1	—
22	2·2	20 or more
23	—	15
24	2·3	—

In *Case* 2 there is no evidence that the section from the proximal part was chosen because of apparent severe stenosis.

In addition to these cases with extramuscular diverticula, *Case* 20 (intramuscular diverticulum) had an obviously distended main lumen filled with mucus; the internal circumference in a proximal part was 2·7 mm.

The readings obtained by measurement of sections through diverticula suggest that the lumina were there considerably expanded. But it may not be so; for these sections may run obliquely across the lumen in a place where it is angled like a U (cf. *Experiments* 4, 8, 9).

One must remember (and this is a matter usually overlooked) that a constriction of the lumen cannot be regarded as an obstruction *per se* without reference to the viscosity of the contents and the strength of the muscle. Appendices with diverticula are often apparently empty; the contents when present are similar to those of appendices without diverticula. But it is probably fair to conclude that: (*a*) A reduction of the lumen to 4·0 mm. internal circumference or less is likely to function as an obstruction; (*b*) Such a constriction may operate in the formation of extramuscular diverticula.

3. ON THE ROLE OF MUSCULAR ACTIVITY

Muscular Activity essential to Diverticulum Formation.—The views of Stout (1923) and Edwards (1934, a, b; 1939) have already been quoted. The experiments reported above show that when diverticula were formed at artificial openings there was always a synchronous muscular contraction; while, on the other hand, if the muscle did not contract, either for some unknown reason or because it was prevented by stretching or distension, then diverticulum formation was minimized or totally inhibited.

From these findings, as from those of Stout, as well as from such phenomena as complete diversion of the lumen, one can only conclude that muscular activity is essential to the development of the common morphological forms of extramuscular diverticula.

The Relationship between Distension and Muscular Activity.—We have now arrived at this curious position: Simple distension cannot produce these diverticula; but stenosis sufficient to cause distension may play a part in their development. Moreover, muscular activity, which experimentally was inhibited by distension, is essential to their development.

It seems to me that these apparently conflicting elements may be reasonably synthesized in this way: The pressure inside any space is the product not only of the nature or behaviour of its contents but also of the nature or behaviour of its walls

In the appendix, the pressure in the lumen is the product of a distending force (such as the force of mucus secretion) on the one hand, and of a compressing force (the contraction of the muscularis) on the other hand.

In fact, the intra-appendicular pressure is not simply the pressure in the lumen; it is really the intramuscular pressure.

Accordingly, extrusion of part of the contents of the muscular tube through some point in the wall of that tube will depend on the relation between the strength of the wall and the pressure in the tube. That pressure (the intramuscular pressure) will vary from moment to moment with the contractions and relaxations of the muscle.

If a breach is forced in the wall, the contents of the tube will be extruded until the intramuscular and extramuscular pressures are balanced; which may be soon or late.

In my experimental diverticula it was observed that their appearance was dependent on the ability of the muscle to contract, and was accompanied by the appearance of mucosal rugosities, by angulation of the lumen at the diverticulum, and by shortening of the appendix. But where, on the contrary, the muscle was prevented from visibly contracting, there were no rugosities, any slight bulging into artificial openings was smooth and gently curved, and there was marked lengthening of the appendix. These artificially-produced states are in each case the product of artificially extreme circumstances seldom if ever found in the natural order of things; for in the first case there is unopposed muscular activity, while in the second there is such opposition that the muscular activity is unable to have any effect.

Turning now to naturally occurring diverticula, we observe that the muscle is hypertrophic in nearly all of them (*see Table I*). This would be expected, as the natural result of the attempt to push accumulated contents through a proximal stenosis. And the natural result of the hypertrophy would be that the intramuscular pressure would depend in increasing proportion on muscular activity; in decreasing proportion on accumulation of contents. Again, in naturally occurring diverticula mucosal rugosities are sometimes marked, sometimes absent; and angulation of the lumen is common, reaching an extreme form in complete diversion.

Summing up, the morphology (expansion of cavity, mucosal rugosities) of the part of an appendix distal to a constriction will depend on the relation between the expanding force exerted by the contents and the compressing force exerted by the muscle; and the morphology of extramuscular diverticula arising in such appendices will vary according to the morphology of the various structures just before the extrusion of the diverticulum, and the relation between the intramuscular and extramuscular pressures at the time of the extrusion and from time to time thereafter.

Applying this idea to specific cases, it seems possible that in *Case* 8 (*Figs.* 69–71) the expanding force was superior to the compressing force, for the rugosities are smoothed out, and the diverticula are smoothly and gently curved; but the hypertrophy of the muscle shows that it, too, has played a part.

In *Case* 19 (*Figs.* 80–84) it may be suggested that in the early attack of appendicitis there was serious damage to the muscularis at the point where the diverticulum was later to appear. This weak point gave way very readily, before a pressure unusually low because mucus secretion was scanty and muscle hypertrophy was not produced. (This appendix was probably removed unusually early in the history of the diverticulum.)

In *Case* 17 (*Figs.* 78, 79) the compressing force exerted by the muscle was superior to the expanding force of mucus secretion, for luminal distension is slight; and the intramuscular pressure resulting from the combined operation of these two factors could not break down the fibrous bulkhead obliterating the lumen, but could break down the apical opening. Thus the contained mucus was pushed out through the apical opening like tooth-paste out of a tube.

Variations in the different factors may in such ways be held to account for the findings in the other extramuscular examples.

In the cases reported radiologically, where there has been apparently no constriction, it may be suggested that inflammation had produced a zone in the wall of such weakness that the normal intramuscular pressure, without the augmentation produced by a stenosis, was sufficient to extrude the diverticula.

Summary.—In brief, stenosis leading to distension combines with muscular activity in the formation of most extramuscular diverticula of the appendix. Their formation is possible apart from the operation of stenosis and distension; but, if muscular activity be excluded, their development is not possible.

4. ON THE ROLE OF INFLAMMATION

The Limited Value of Certain Histological Features.—Numerous authors have discussed the part played by inflammation in the development of diverticula. The views put forward are sometimes apparently contradictory (Hansemann, 1896; Letulle and Weinberg, 1897; Mertens, 1902; Mundt, 1903; Lejars and Ménétrier, 1904; von Brunn, 1905; Aschoff, 1908; Maalöe, 1908; Malatesta, 1908). For example, one view was that vascular openings predisposed to the development of inflammatory diverticula; another that only non-inflammatory diverticula passed through vascular openings. Clearly the terms 'inflammatory' and 'non-inflammatory' have not been used in comparable senses; in the first case it is implied that the vascular openings come at the end of a sequence of causal factors, of which inflammation is the chief, in the second that inflammation did not produce the openings in the muscle.

Vascular Openings and Fibrosis.—In the present series 18 appendices with extramuscular diverticula were examined microscopically, whereby 16 were proved to contain diverticula passing through vascular openings. Submucous fibrosis in excess of normal was present in every one of these sixteen,

and also in both examples where the diverticula were not proved to pass through vascular openings (*See Table I*). One must conclude that fibrosis and vascular openings are not useful distinguishing features.

The Muscularis Mucosæ.—On the absence of the muscularis mucosæ as an indication of past inflammation, let it suffice to say that this structure is present in a high proportion of appendices with strong evidence of previous or chronic inflammation. Moreover, the muscularis mucosæ is present in a high proportion of the diverticula in this series, including some which by certain criteria would be called ' inflammatory '.

The Mucosa and Submucosa.—The nature of the mucosal and submucosal layers surrounding diverticula is likewise no indication of the manner of their development, and so of their type ; for the so-called ' inflammatory ' and ' non-inflammatory ' types could probably become more and more alike with passage of time. Bérard and Vignard (1914) pointed out that a diverticulum originally lined by normal mucosa might by inflammation come to resemble one produced by epithelialization of an abscess cavity. Morphological resemblance might be brought about in the other direction, for the remarkable reparative and hyperplastic powers of epithelium and lymphoid tissue permit the development of ' good ' mucosæ and submucosæ (given time) from very small beginnings.

Muscle in the Walls of Diverticula.—Von Brunn (1905) and Aschoff (1908) thought that diverticula resulting from inflammatory damage have muscle in their walls carried out from the edges of the breach in the muscularis. The following observations indicate that such findings have little or no significance.

In the course of this work sections were prepared and examined from 143 slices cut from 51 appendices which did not show diverticula. Muscle-bundles were found outside the main muscular coat in 32 of the 143 blocks. These bundles were nearly always found in the meso-appendix, in some cases as much as 1 cm. distant from the outer margin of the muscularis ; they were occasionally found at the apex, rarely anywhere else. As it must be admitted that ' inflammatory ' diverticula (in even the restricted sense of the term, which means that the muscle had been weakened by inflammation) can occur on the mesenteric border, the finding of muscle in the walls of diverticula probably means only that the diverticulum had been formed at a place where muscle had previously existed outside the main muscle coat.

Some other features of these ' extramuscular ' muscle-bundles are of interest. They nearly always lay close beside nerves or vessels. In some cases without diverticula they were seen to be continuous with the main muscular coat, and to arise from it at vascular openings. Similar prolongations of the muscularis have been observed also in cases with diverticula ; for examples, *see Figs.* 85, 86, 89.

These muscle-bundles are surely normal anatomical structures, although they are not mentioned in the standard anatomy and histology books. Their being so often associated with nerves recalls the musculo-nervous complex of the submucosa described by Masson (1930). He observed slender muscle-bundles running obliquely from the inner aspect of the main muscularis across the submucosa to join the muscularis mucosæ, these bundles being commonly accompanied by non-medullated nerve-fibres. This complex was more richly developed in appendices showing the submucous fibrosis usually associated with chronic inflammation.

Possible Significance of Musculo-nervous Complexes.—One may perhaps speculate on these internal and external musculo-nervous complexes in another context. Edwards (1934, a) demonstrated in the colon alternating bands of hypertrophy and atrophy in the circular muscle coat ; and he thought they were due to disorder of its function, and were important in the development of diverticula. He thought that some disorder of muscular contraction might also play a part in the development of appendicular diverticula, though there is no morbid anatomical feature in the appendix comparable to that described in the colon. I do not see that it is necessary, on the evidence available, to postulate any disorder of muscular action other than an increase in its force ; but the facts (of the existence of these musculo-nervous structures, of the more marked development of the submucous complex of Masson in fibrotic appendices, and of the marked fibrosis found in cases with diverticula) make one wonder if possibly chronic inflammation causes dysfunction or hyperfunction favourable to the appearance of diverticula.

Conclusion.—The knowledge at present available does not justify a conclusion more advanced than this : that in the development of the common morphological forms of diverticula inflammation plays little or no part beyond producing constriction of the lumen.

Classification : I do not think that the state of our knowledge justifies the description of more than three types—Congenital, Acquired, and Others of Unknown Origin.

V. SUMMARY

1. In the literature on diverticula of the appendix much confusion is revealed, especially on the significance of certain histological details, and on the role of passive distension. The function of the muscle is largely overlooked.

2. Histological and experimental evidence is brought forward to show that muscular activity is indispensable to the formation of extramuscular appendicular diverticula.

3. ' Intra-appendicular pressure ' should be called ' intramuscular pressure ', and is affected more by muscular activity than by passive distension by accumulated contents.

4. Increase of intramuscular pressure is initiated usually by accumulation of contents behind a constriction, and maintained by muscular activity and hypertrophy.

5. The morphology of extramuscular diverticula depends on the morphological and pressure relationships of structures inside and outside the muscular tube immediately before, at, and after the time of their formation.

6. The role of inflammation is in most cases probably confined to the formation of a constriction.

7. Microscopy is essential to prove total fibrous obliteration of the lumen.

8. Some extramuscular diverticula develop in the absence of stenosis.

9. Certain histological details, once thought to identify various types of diverticula, are shown to be valueless.

It is a great pleasure to record my thankfulness to my chief, Professor W. D. Newcomb, for his encouragement, valuable advice, and kindly criticism. I am indebted also to several surgical colleagues and to the nursing staff for pleasantly tolerating my activities in and around the theatres. I also wish to thank Mr. D. Morritt for doing a proportion of the technical work involved.

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CHANGES IN CARCINOMA OF THE BREAST FOLLOWING IRRADIATION

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DURING the past three years there has been an opportunity at Westminster Hospital to study the effect of irradiation on cases of carcinoma of the breast which have been treated by means of high-voltage X rays applied to the tumour area and subsequent radical mastectomy. In most cases a biopsy has been obtained before therapy was instituted, and in those cases where ulceration had occurred, serial biopsies were taken during the course of irradiation. In a few cases no pre-irradiation biopsy was available and it might be argued that no proof of carcinoma existed. It is clear, however, that if malignant cells were demonstrable in the specimens obtained from the ensuing radical mastectomy, then such cases are significant in the assessment of results.

The purpose of this report is to set out the structural changes which occur in the malignant tissue of the breast as a result of high-voltage X-ray irradiation. It should be made clear that there is no attempt at this stage to suggest any particular mode of treatment for this disease, nor is any account taken of the changes in metastatic deposits, in particular those of the axillary lymph-nodes, which will be dealt with in a separate paper. For this reason no assessment of prognosis is made in the cases under discussion.

History.—Since 1895, when Professor Roentgen in Wurzburg discovered the rays which bear his name, many students in the fields of physics and biology have applied themselves to the elaboration of his work. With the knowledge gained at first accidentally by Becquerel, and as a result of planned experiments by Curie (Becquerel and Curie, 1901), that roentgen rays had a destructive action on living tissue, the field lay open for investigations into the nature of the cells most easily destroyed and the manner of their destruction. Curie and Becquerel, with the aid of the French physicians Bouchard and Balthazard, developed the conviction that by destroying neoplastic cells radium and roentgen rays could be used in the treatment of malignant disease. Since that time the result of the study of the biological effects of irradiation on normal and malignant tissues has led to the belief that cell changes may occur in one of two ways :—

1. As a result of a direct action on a cell.

2. By an indirect action on the cell produced by restriction or inhibition of local blood-supply. Bergonié and Tribondeau (1906), basing their views on changes observed in the testicle, were among the first to express the belief that the effect was directly on the cells. The striking results obtained by irradiating tissue which is proliferating rapidly has led to the view that cell death occurs as a result of degenerative mitosis (Lacassagne and Monod, 1922 ; Nabias, 1928), a theory opposed by Donaldson and Canti (1923) and Cheval and Dustin (1931), but more recently revived in the light of knowledge gained of the effect of irradiation on chromosomes, which indicates that there can be little doubt that irradiated cells may die when division is attempted (Spear, 1946).

The effects on cells in tissue culture has given evidence of the indirect reaction upon embryonic tissue, and Strangeways and Fell (1927) have suggested that absence of gaseous exchange in the tissues resultant upon arrest of blood-flow is an important cause of cell death. They also showed that the dosage necessary to produce indirect cell death was higher than the dosage required to produce a direct effect upon the cell. The results following blood-supply changes are conspicuous (Harvey, 1942), and impressed by the vascular changes in the irradiated tissues many workers have suggested that the main cause of cell change following irradiation is the result of impaired blood-supply (Bashford, Murray, and Cramer, 1905 ; Pullinger, 1932). This view can be refuted by reducing the dosage below that necessary to produce vascular changes and at the same time being able to demonstrate that cell alteration still occurs (Desjardins, 1932).

The vascular obstruction effect cannot be disregarded, and its role has been well demonstrated by irradiating embryos *in ovo* before and after the circulation is established (Wilson, Hughes, Glucksmann, and Spear, 1935). So long as circulation is intact, recovery from direct effect occurs, whereas when the blood-supply is inadequate, subsequent cellular change on further irradiation is considerably greater.

It may be said, therefore, that at the present time the majority of workers feel that cell death following irradiation results from a variety of causes which may be grouped under the general headings of direct effect on the cell, and indirect effect by obliteration of blood-supply. The exact mechanism of cell death is as yet not understood, although several theories have been put forward. It is interesting to note that these conclusions are much the same as those reached in an excellent review by Ewing as long ago as 1926.

A more recent method of approach to changes in malignant tissue following irradiation has been that of Glucksmann (1941 and 1946) and Glucksmann and Spear (1945), who have set out to determine how many types of cell change can be recognized by the examination of cytology in material obtained by serial biopsies taken from squamous-cell carcinomata undergoing irradiation therapy.

PLAN AND TECHNIQUE OF INVESTIGATION

Most detailed studies of cellular changes in malignant tissue following irradiation have been made on squamous-cell carcinoma, presumably because from these tumours it is easiest to obtain material for histological examination.

The majority of work done on breast carcinoma has been in America, but in a review of the literature no really detailed account of histological changes in a large series has been found. Adair and Stewart (1935) and Adair (1936 and 1939) have reported 65 cases treated by high-voltage X rays pre-operatively. Histological descriptions were meagre, however. These authors state as a general conclusion that in their series 33 per cent of cases showed complete disappearance of carcinoma cells after irradiation. It is not clear from their papers, however, what exactly were the doses employed in individual cases. Halley and Melnick (1940) have given a review of 21 cases with a good account of histological changes and Lee and Herendeen (1924) and Pfahler (1938) have considered the problem principally from the purely clinical point of view.

The present account is based on 60 cases, from which 74 specimens in the form of either biopsies or mastectomies were received.

They may be grouped as follows :—

Group 1 : Cases where skin ulceration had occurred and multiple biopsies were carried out at varying doses during treatment.

Group 2 : Cases where a biopsy not amounting to local excision of the tumour was performed before irradiation.

Group 3 : Cases where a biopsy which did amount to local excision of the tumour was performed before irradiation.

Group 4 : Cases where no biopsy was performed before irradiation.

In all the cases the breast was subsequently made available for study as a whole, when radical mastectomy was performed.

It is clear that in Groups 1 and 2 complete experimental control is achieved in that diagnosis was made before treatment, and a study of comparable tumour material was possible after irradiation.

In Group 3 it might be argued that local excision of the lump could have removed all the existing carcinoma within the breast at that time, and therefore a failure to find tumour cells at subsequent mastectomy could not be claimed as a result of irradiation. This was a group of 5 cases, and in every instance the results were made significant by the finding of malignant cells either normal or altered in the tumour area after mastectomy.

In Group 4 the criticism of failure to establish a diagnosis of carcinoma might be levelled. In all these cases, however, proof beyond doubt of pre-existing carcinoma was obtained, either by the presence of metastases in the axillary lymph-nodes, or by the finding of carcinoma cells in the breast itself at mastectomy.

The irradiation of all the cases studied was performed at Westminster Hospital by the technique of Allchin and Wilson, Method I (1948). This manner of treatment achieved a maximum degree of uniformity of dose throughout the entire tumour mass by making use of a 'pre-determined shape' method (Green, 1943). The high-voltage X rays were generated at 220 kv., using a filter of 2 mm. copper and 1 mm. aluminium, with focal skin distance (F.S.D.) of 50 cm., and half-value layer (H.V.L.) of 2·2 mm. copper.

The majority of cases received a total tumour dosage of between 2000 r and 4000 r, but in those cases where multiple biopsies were performed it was possible to observe the effects of lower dosage.

The rate of dose was, within limits, constant, thus :—

Dosages of 2000 r to 2500 r were administered in 20 to 25 days.
Dosages of 2500 r to 3000 r were administered in 25 to 35 days.
Dosages of 3000 r to 3500 r were administered in 30 to 36 days.
Dosages of 3500 r to 4000 r were administered in 36 to 40 days.

For the purposes of assessing histological change, therefore, it is proposed to regard the tumour dose rate as constant.

The variables to be considered are : (1) Relative sensitivity of different tumours ; (2) Total tumour dose.

In a series such as this it is impossible to make any useful contribution as regards sensitivity of individual carcinomata to irradiation, in terms of histological appearances. A very large total number with careful correlation of each histological type to various dose levels would be required. This point was made clear by Ross (1939) when studying the effect of gamma irradiation by radium needles in carcinoma of the breast. Further, the opinion has been formed, based on the routine study of breast carcinoma in this department, that no basis of histological classification is very satisfactory when applied to the grading of mammary cancer. In this connexion it is considered of importance to point out that in every one of the cases in this series where a dosage in excess of 3500 r was given, maximal cellular change occurred in the tumour area, whereas only occasionally were comparable changes found with doses below this level. The occasional finding of considerable tumour destruction at low dosages gives convincing evidence that some mammary cancers are more sensitive than others, in common with malignant disease elsewhere. However, a constant finding of maximum benefit from higher doses seems to indicate that it would be of greater value to concentrate attention on irradiation methods which can deliver high tumour doses with minimal damage to normal tissues, rather than to make an attempt, by histological means of doubtful value, to pick out those cases which might be sufficiently sensitive to benefit from lower dosages.

When sufficient cases which have been treated at the upper dosage levels are available for study, it might be possible to extract those which do not respond even to a very high dose, and thus possibly to correlate histological appearances with radio-resistance.

The general law that above a certain dosage large numbers of tumours will react to irradiation, whereas lower dosages will produce occasional results, presumably in the more sensitive cases, has been clearly stated by Paterson (1948).

In assessing cellular changes in malignant tissue as a result of varying total tumour dosage a further point must be taken into consideration—namely, the length of time which has elapsed between completion of irradiation and either biopsy or mastectomy. It is clear that in cases where material is seen very shortly after irradiation, changes may not have had time to develop ; and at the other extreme, if a very long time has elapsed, viable cells

remaining after irradiation may have had time to proliferate (*Fig.* 99). This point has been stressed by Halley and Melnick (1940).

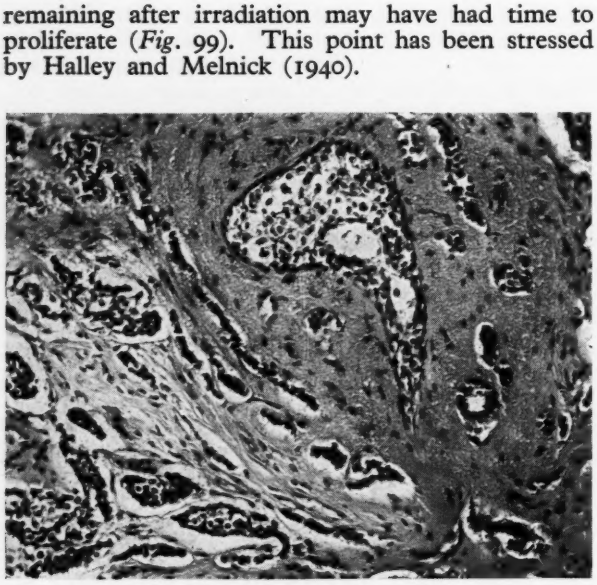


FIG. 99.—Re-growth of carcinoma cells with evidence of old irradiation change around duct. Material from mastectomy performed 94 days after completion of irradiation. (× 110.)

Technique.—With these features in mind the following plan of study has been adopted: All specimens have been fixed in 4 per cent formol-saline. Material for study has been carefully selected from all parts of the breast, so that an average of 5 to 6 blocks have been made from each case. In addition one or more whole breast 'giant' sections have been taken, so that a general impression of changes taking place throughout the breast could be obtained.

NAKED-EYE CHANGES

It is not proposed to give any details of measurements of tumours in individual cases, neither will any assessment of shrinkage following irradiation be attempted. It is considered that measurement of tumour size in the breast is so inaccurate that no useful conclusions can be drawn.

Skin changes will not be given in detail, for these have been well described elsewhere (Cade, 1940), and the findings in this series were quite typical.

Slowly increasing erythema was seen after a dosage of 2000–2200 r, becoming intensely scarlet at 2700–3000 r. At about this dose surface desquamation usually commenced (dry peeling) and at 3300–3500 r small vesicles appeared, which quickly burst (moist peeling). Healing usually was visible to the naked eye within fourteen days of the commencement of moist peeling, and was complete in 90 per cent of cases in from two to five weeks. The histological changes in the skin in cases which had received adequate irradiation were typical, showing flattening of rete pegs, thinning of the epidermis, and atrophy of the skin appendages. Desquamation or underlying fibrosis was seen, according to the stage at which the specimen was received.

Naked-eye appearances of the cut surface of the breast showed, in cases where there was little or no response to irradiation, the usual findings of carcinoma. Where irradiation changes had taken place the tumour area tended to merge into the surrounding structures and was sometimes difficult or impossible to locate except as an area of increased resistance to the examining finger. In nearly all cases there was a generalized enlargement of the corpus mammæ, presenting a greyish colour and an extremely tough consistency.

Diminution of total breast substance was a common finding, and occasionally marked contraction with virtual disappearance of fat was seen.

HISTOLOGICAL FINDINGS

The tumour changes as seen by histological methods are discussed under two broad headings, namely: (*a*) Cellular effects; (*b*) Connective-tissue changes and replacement phenomena.

Cellular Effects.—The most striking change noticed was the actual disappearance of malignant cells following irradiation, which seems to take place in one of the following ways: (1) Acute cell dissolution, either immediate or delayed; (2) Alteration of cell structure followed by death.

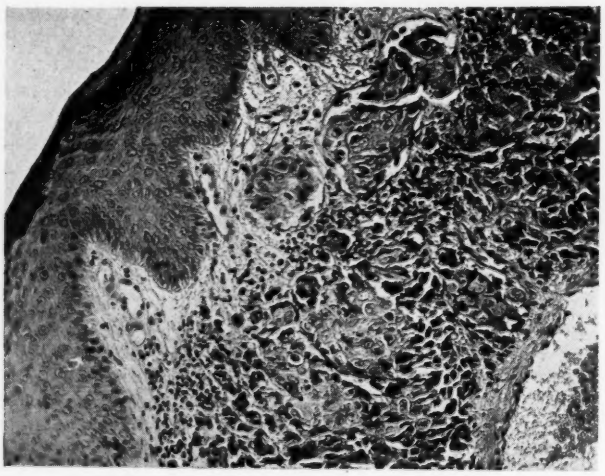


FIG. 100.—Biopsy from an ulcerating carcinoma taken before irradiation was commenced, showing a diffuse anaplastic carcinoma simplex. (× 105.)

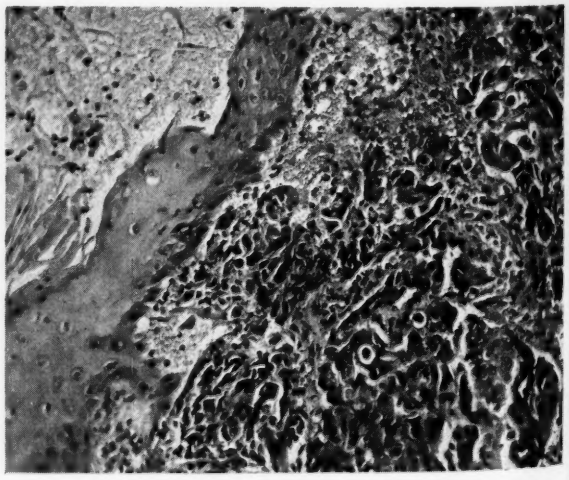


FIG. 101.—Biopsy taken after 2000 r showing no appreciable change other than some œdema of malignant cells. (× 105.)

Cell Dissolution.—In different tumours varying numbers of malignant cells die and disappear from the tissue according to the sensitivity of the individual neoplasm. A certain number of cells are killed and removed rapidly, whilst others remain without showing any specific microscopical changes until at a higher dosage or after a longer period of time they also undergo necrosis. These changes can be well followed by studying multiple biopsies taken from the same tumours after varying dosages. A series showing changes in such a case is found in *Figs.* 100–103.

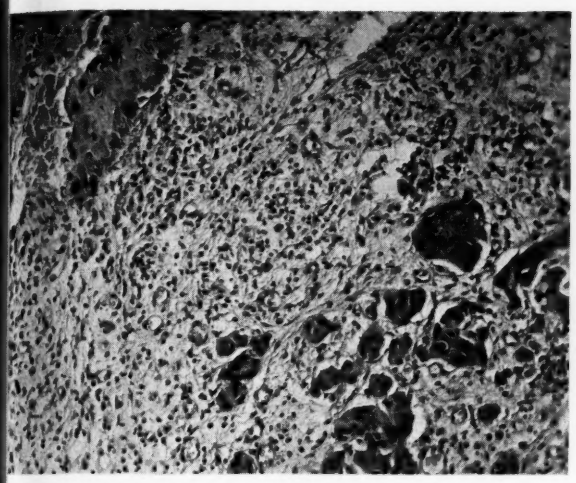


FIG. 102.—Biopsy taken after 2500 r, showing a marked diminution in the number of malignant cells present, together with synplasm formation of the remaining cells. The substrate is laid bare and shows the appearance of granulation tissue. (× 105.)

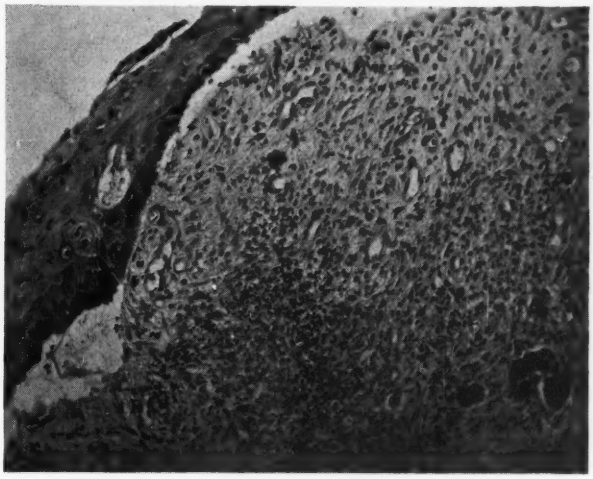


FIG. 103.—Biopsy taken after 2950 r, showing a further diminution of the number of malignant cells, together with an invasion of the substrate by inflammatory cells. The flattening of the rete pegs of the overlying skin may be noted. (× 105.)

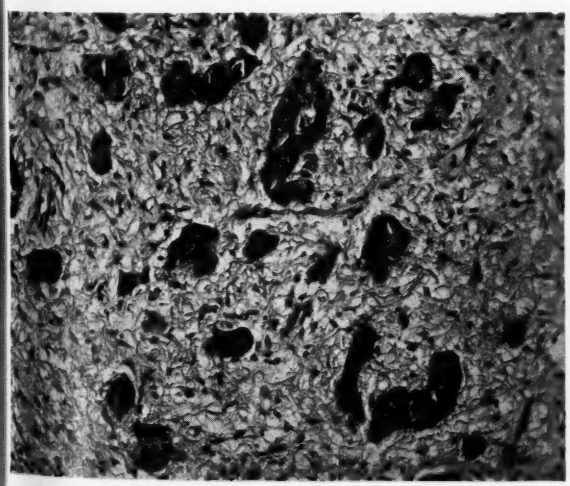


FIG. 104.—Biopsy taken immediately following 3000 r, showing synplasma and loose connective tissue. (× 105.)

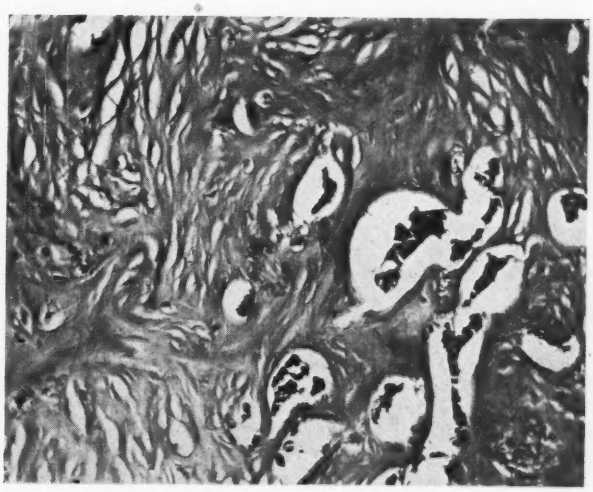


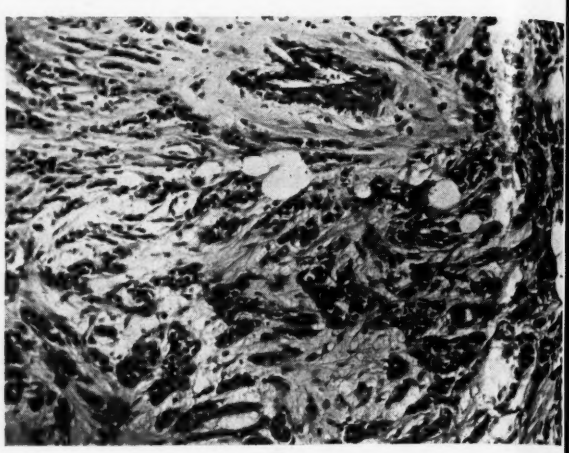
FIG. 105.—Biopsy from the same case 49 days later —no further irradiation had been given. It shows pyknotic cells and densely hyaline connective tissue. (× 105.)

A point of importance which may be stressed is that some malignant cells seen remaining in a biopsy specimen taken soon after irradiation therapy has finished may disappear after a time interval even though no further irradiation has been given (*Figs.* 104, 105). Clearly such cells must be fully differentiated and incapable of further reproduction. In the breast no specific histological features are recognizable in this type of cell, such as the keratinization found in the squamous cells of skin carcinomata.

Glucksmann (1941 and 1946) has made use of the appearances of differentiation in squamous-cell carcinoma as one of the indications of radio-curability. No comparable features have been discovered in carcinoma of the breast, as was to be expected in view of the nature of the cells. This, however, is of little practical importance, for except possibly in those tumours where skin ulceration has taken place, and these provide only a small number of total cases, it would not be feasible to attempt any method involving multiple biopsies in order to assess irradiation effect.

A significant feature would appear to be that in all the cases studied receiving a dosage higher than 3500 r very considerable tumour destruction occurred,

A



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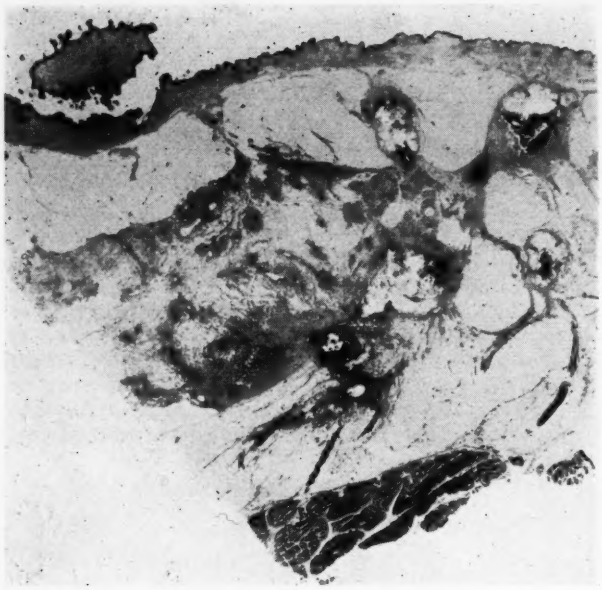

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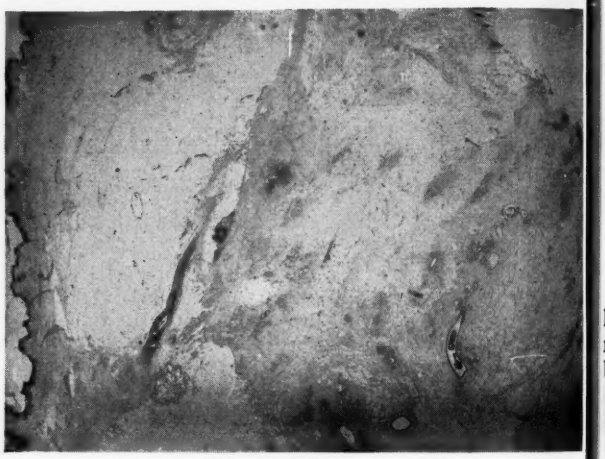


D

FIG. 106.—A, 'Giant section' of a slice of breast, taken through the nipple and underlying tissue before irradiation. (× ¾.) B, Shows the histology of the tumour. (× 100.) C, 'Giant section' taken at the site of the original slice biopsy when radical mastectomy was performed following irradiation (3680 r). (× ⅜.) D, Photomicrograph of the tumour area after irradiation, showing disappearance of tumour cells. (× 50.)

A

B

FIG. 107.—A, Macroscopical photograph of 'giant section' of slice biopsy through nipple and underlying tissue, showing an intensely staining area which histologically was a carcinoma. (× ¾.) B, Macroscopical photograph of 'giant section' of mastectomy specimen removed 35 days after 3780 r, given in 46 days. The tumour area was in the zone of scar tissue seen to the right of the nipple. No viable malignant cells were found. (× ½.)

amounting in 4 out of 11 cases to complete disappearance of malignant cells (*Figs.* 106, 107), and in the 7 remaining cases only grossly altered cells, of a type which will be considered later, were demonstrable histologically after careful search.

The actual mechanism of acute cell dissolution seems to be principally by lysis of both nucleus and cytoplasm, although some examples of pyknosis and karyorrhexis of the nucleus are seen. The exact nature of cell break-up has been well demonstrated by Ludford (1932).

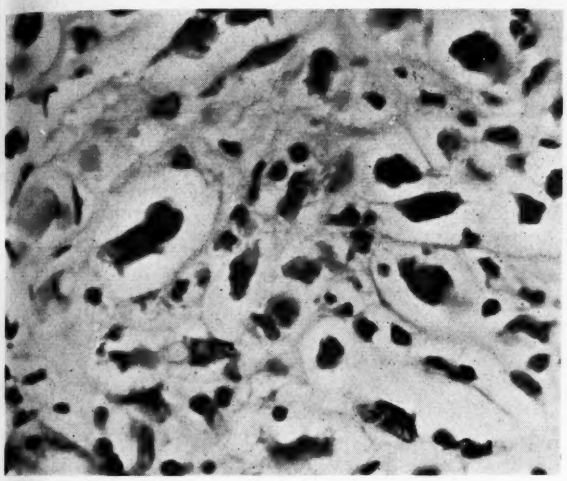


FIG. 108.—Pyknotic and giant nucleated cells from a mastectomy specimen. Dosage 3000 r. (× 390.)

FIG. 110.—Nuclear vacuolation and giant-cell formation. (× 400.)

Alteration of Cell Structure.—The alterations in cell structure which may occur following irradiation are numerous. Mention has already been made of the presence of fully differentiated cells incapable of division. It may be assumed that together with increase of fully differentiated cells there would be a diminished number of cells undergoing division. Any attempt to assess irradiation effect by estimating a reduction in number of mitosing cells is impracticable in the breast, however, as in the majority of mammary carcinomata the presence of active cellular division is not a feature.

Degenerative changes: The cell changes which can be demonstrated are quite clear-cut, and it has been suggested by some authorities (Crowther, 1938) that they represent a fundamental mutation-like alteration.

Nuclear changes include a tendency to pyknosis on the one hand, and enlargement with or without vacuolation on the other.

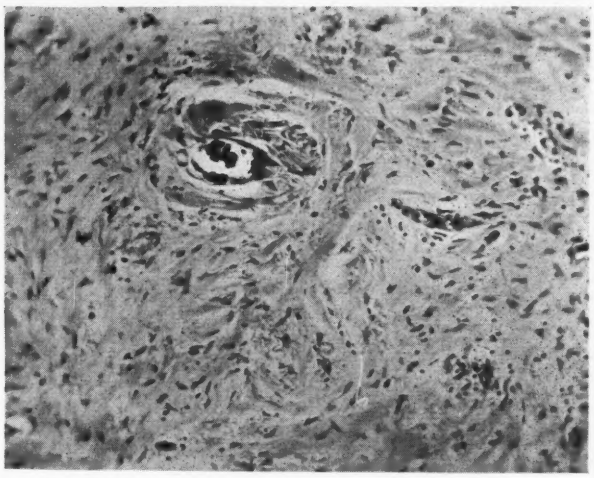


FIG. 109.—Small pyknotic cells. The only remnants found in a mastectomy specimen from a case which had received 3680 r. (× 110.)

In mastectomy specimens where the vast majority of tumour substance has disappeared it is common to see small pyknotic nuclear remnants (*Figs.* 108, 109). A type of nuclear enlargement is seen where there is a conglomeration of chromatin to produce an intense hyperchromatic appearance with loss of normal pattern-work. Nuclear vacuolation is occasionally seen (*Fig.* 110).

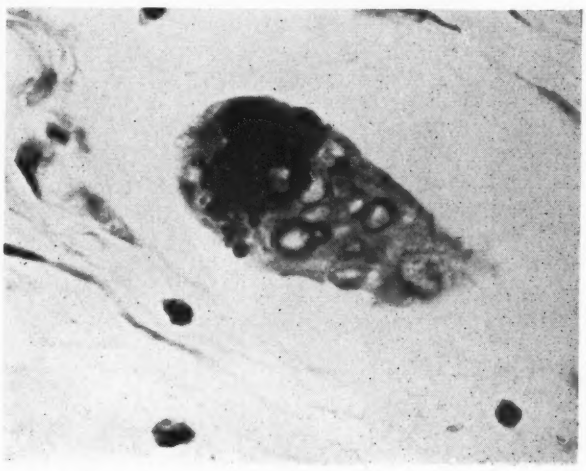


FIG. 111.—Cytoplasmic vacuolation. (× 750.)

Cytoplasmic and cell membrane changes: Vacuolation also occurs in the cytoplasm, together with a foamy transformation of the cytoplasmic substance (*Fig.* 111). Such cells give negative results when stained by dyes specific for fat, and the suggestion of Failla (1940) and others, that following irradiation the permeability of the cell membrane is altered and

fluid is absorbed into the cell, seems reasonable. The alteration or destruction of cell membrane can also be demonstrated by the frequent appearance of isolated cells where the cytoplasm is seen ' streaming ' from its normal confines (*Fig.* 112). Another

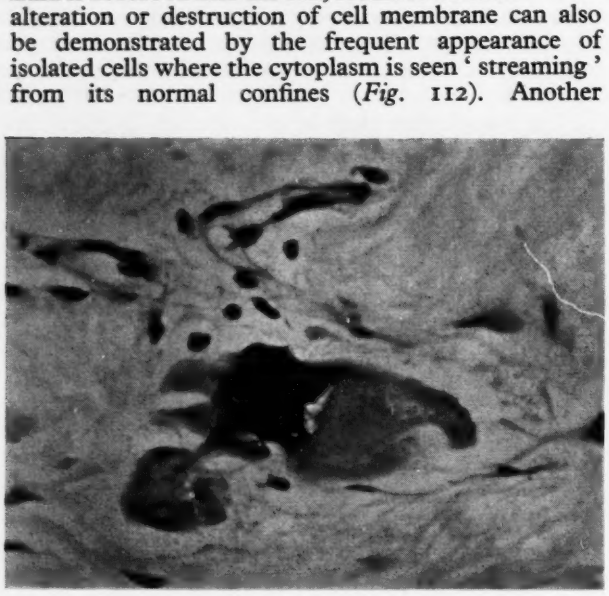


FIG. 112.—Cell showing cell-membrane destruction giving an appearance of ' streaming '. (× 400.)

feature which is almost constantly found in tumours which have been irradiated is a tendency for the cells to run together to form synplasma (*see Figs.* 102, 103), a further evidence of cell membrane damage. In such cells the cytoplasm tends to take on a plum colour when stained with eosin.

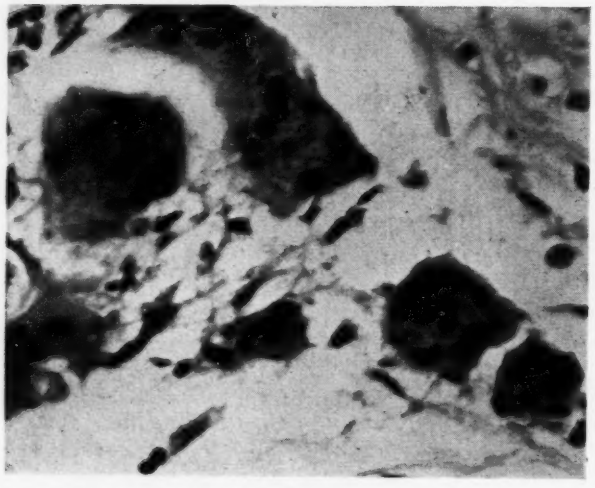


FIG. 113.—Showing giant cells. (× 400.)

Giant cells in irradiated tumours have been described by many authors (Halley and Melnick, 1940; Hall and Friedman, 1948). These were seen commonly in this series, either as large cells with a single dense hyperchromatic nucleus, usually without clear-cut chromatin network, or as multi-nucleated cells, many of which seem to occur as a result of the general tendency to synplasm formation (*Figs.* 113, 114).

Calcification: Melnick and Bachem (1937) and Halley and Melnick (1940) have stressed the finding of calcification in irradiated tumours and have suggested that in those cells which do not undergo acute dissolution, death occurs as a result of nuclear calcification. Hall and Friedman (1948), studying squamous-cell carcinomata, did not find calcification to be a significant change.

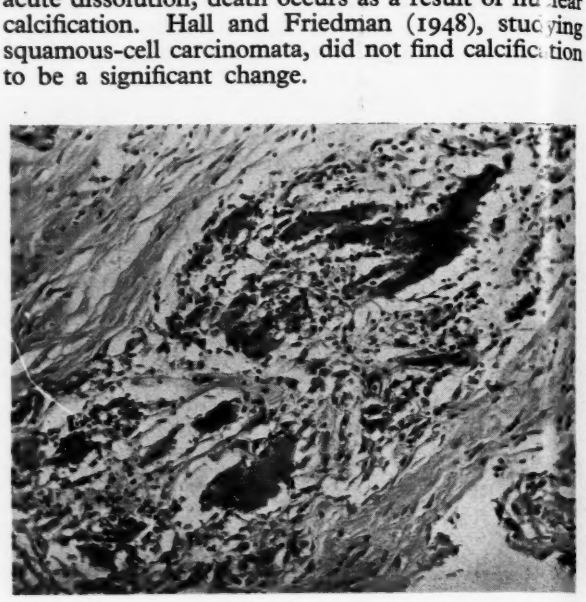


FIG. 114.—Showing giant cells of somewhat different appearance. In both cases these were the only abnormal cells found in this mastectomy specimen. (× 105.)

In the present series areas of calcification were found in 50 per cent of cases, and were sometimes sufficiently diffuse to make the cutting of the ' giant ' sections difficult. The calcium was always distributed in microscopic amounts. It was found sometimes in the nuclei of malignant cells (*Fig.* 115), and frequently was seen lying in the connective tissue, replacing areas of destroyed tumour substance (*Fig.* 116). From the material studied it cannot be said

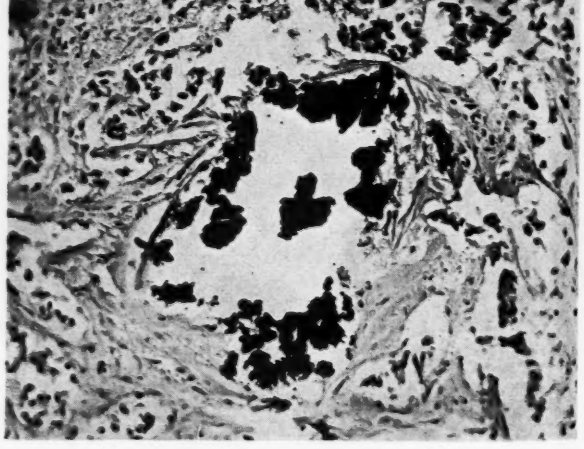


FIG. 115.—Calcification in tumour cell nuclei (Von Kossa staining method). (× 120.)

that the calcium is always deposited in cell nuclei as suggested by Halley and Melnick, although it is significant that whenever seen it was either within the cell or in areas of connective tissue replacement where malignant cells had previously existed. It is not felt, however, that Halley and Melnick's theory

that nuclear calcification is the most significant mechanism of post-irradiation death other than acute dissolution can be considered, as the finding is not constant throughout the tumours, nor is it present in all cases.

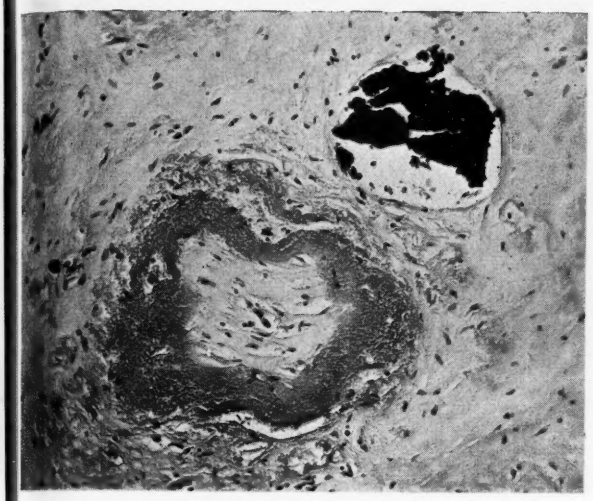


FIG. 116.—Calcification in tumour cell remnants (Von Kossa staining method). (× 105.)

Connective-tissue Changes.—The earliest changes in connective tissue following irradiation have been observed in those cases where biopsies were performed during the course of treatment. As malignant cells disappear the fibrous stroma is laid bare and small capillary vessels are seen dilated (*see Figs.* 102, 104). In the present series the time of appearance of these changes seemed to depend more upon the stage at which malignant cells began to be affected, than upon the actual dosage level or time interval.

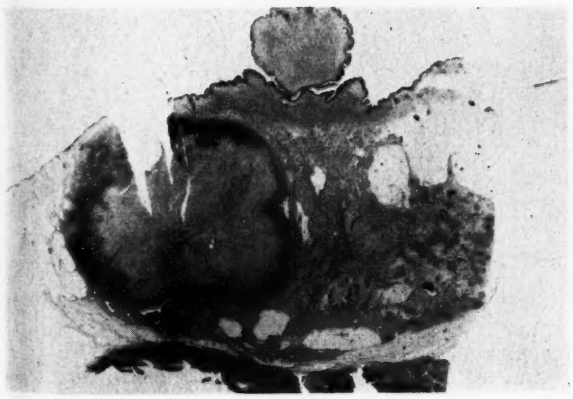


FIG. 117.—Photograph of a 'giant section' of a mastectomy specimen showing an isolated mass of connective tissue replacing a papillary adenocarcinoma which had arisen in a main duct. (× ¾.)

In other words, it was only when the tumour cells had, to some extent, disappeared that it was possible to observe the underlying stroma. This finding is similar to that of Hall and Friedman in squamous-cell carcinoma.

In the cases studied here the lowest dosage causing significant destruction of malignant cells was 2000 r given over 18–22 days.

The ensuing stromal changes closely followed the normal course of repair, in that a gradual increase of fibroblastic activity occurred with the appearance of collagen strands (*Fig.* 117), and the gradual obliteration of small vessels. Of the blood-vessels remaining

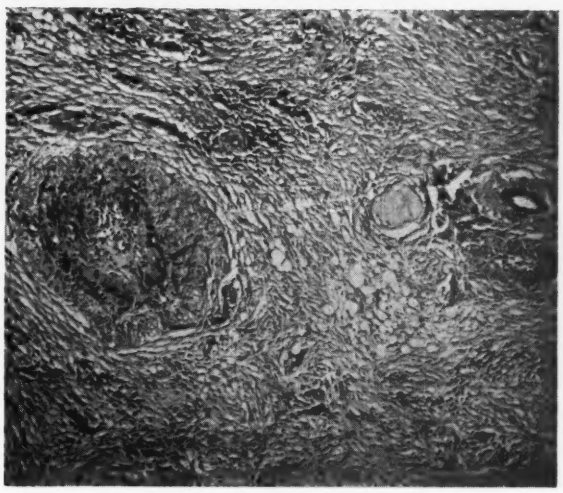


FIG. 118.—Intimal proliferation virtually obliterating the lumen of a small vessel. (× 50.)

it was common to find evidence of some intimal proliferation (*Fig.* 118), but only occasionally in the series studied did this cause lumen obstruction, and only in two cases was vascular thrombosis found (*Fig.* 119). Frequently a deposit of hyaline material, the nature of which will be further discussed later, was found around the periphery of the vessels.

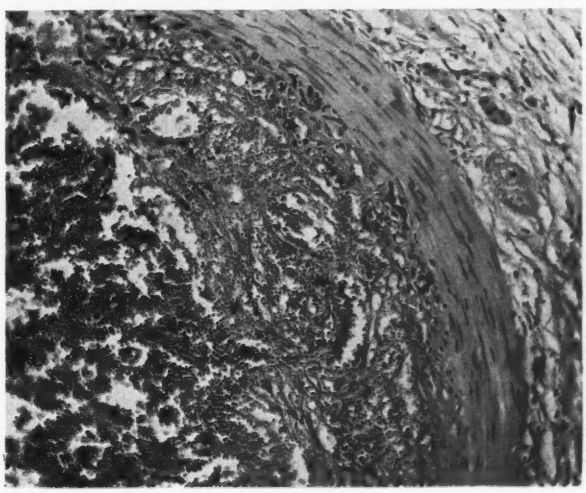
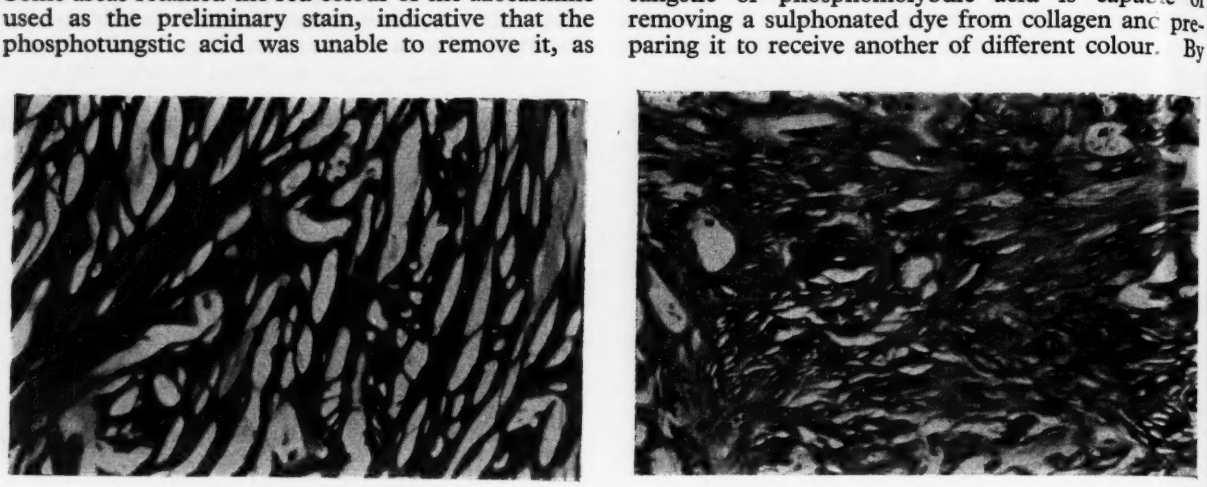


FIG. 119.—Thrombosis with early organization in a moderate-sized vessel. (× 110.)

Certain unusual and hitherto unrecorded features were noted in the formed connective-tissue elements in areas of tumour replacement. When Mallory's phosphotungstic acid aniline blue staining method was used (Mallory, 1938), it was found that among the areas of apparently dense fibrous tissue there were considerable quantities of material which did not give the dark-blue reaction of normal collagen,

but stained either a very pale blue or not at all. Some areas retained the red colour of the azocarmine used as the preliminary stain, indicative that the phosphotungstic acid was unable to remove it, as for its results on Mallory's discovery that phosphotungstic or phosphomolybdic acid is capable of removing a sulphonated dye from collagen and preparing it to receive another of different colour. By



A B

FIG. 120.—A, B, Irregular staining reaction in connective tissue formed following irradiation. (Modified Mallory staining technique.) (× 360.)

it normally does from collagen (*Fig.* 120). On closer observation it was noticed that this tissue stained rather palely with eosin and had that peculiarly structureless character usually described as 'hyaline'. When stained for amyloid, negative results were obtained. The quantity and distribution of this substance varied somewhat from case to case, but increasing the length of time tissues are treated the final colour of the collagen can be intensified. Hyaline, however, stains palely, not at all, or even retains the first dye colour, as described above. By reducing the times to the minimum at which collagen shows a clear-cut colour with the second dye, it has been found that some of the hyaline

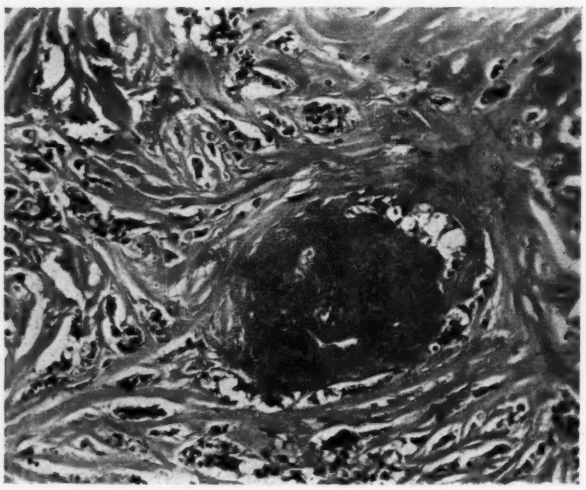


FIG. 121.—'Mass' of debris in area where malignant cells had previously existed. (× 110.)

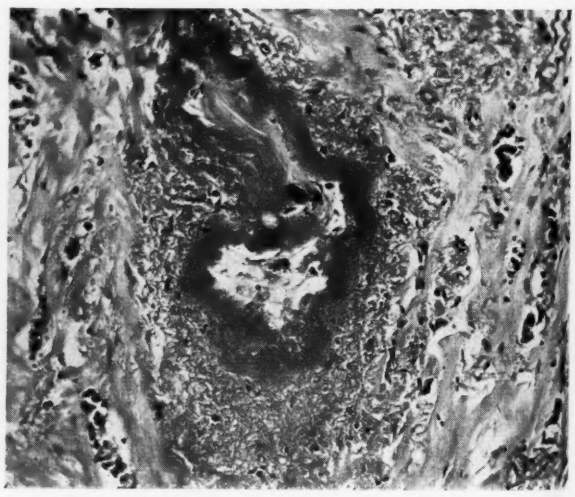


Fig. 122.—Hyaline material and debris lying in the region of a malignant duct. Elastic material can be seen as irregular tortuous strands. (× 110.)

three specific types of deposition were identified. It appears, as already described, scattered through the strands of what is apparently normal collagen. It occurs as larger masses in areas where accumulations of tumour cells have previously existed (*Fig.* 121), and it is found characteristically laid down around the walls of ducts involved in the malignant process (*Fig.* 122). It has not been seen to occur in the normal breast substance, but only in areas affected by carcinoma.

In order to demonstrate this material clearly in histological preparations a modification of Mallory's method has been devised. This technique depends retains the first dye and thus gives a differential stain (*Fig.* 123), whilst some remains colourless (*Fig.* 124).

Thus two types of replacement tissue can be identified in the tumour area following destruction by irradiation :—

1. Thick strands of acellular material apparently collagenous, but which stain very irregularly with aniline blue, and in which many areas retain the primary dye colour (*Fig.* 120).

2. 'Masses' of more granular material sometimes containing scattered chromatin fragments, and

which by ordinary staining methods show wavy strands lying in them, which stain intensely by methods for elastic tissue (*Figs.* 121, 125).

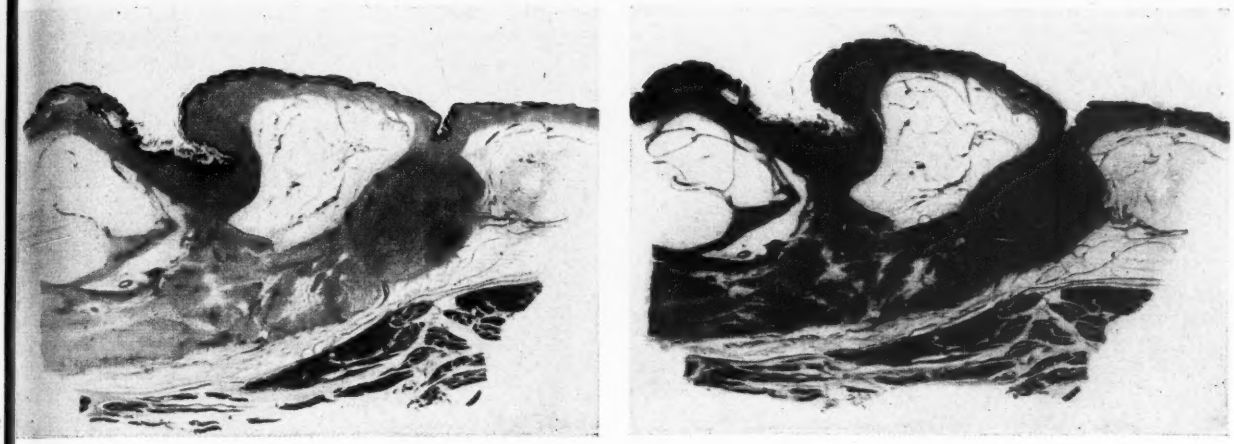
It should be pointed out that the abnormal connective tissue of the first type has not been observed in breast carcinomata which have not received irradiation, whereas the acellular material containing elastic strands is occasionally seen in small amounts more particularly in untreated cases of scirrhous carcinoma, and it may be assumed to be a degenerative process resultant upon inadequate blood-supply.

It is therefore suggested that as a result of irradiation therapy, material of the first type is formed, which is abnormal connective tissue with irregular collagen content, whilst the second type of substance represents a degenerative process and is composed of debris from malignant cells, ducts, and vessels.

Elastic Tissue.—The distribution of elastic tissue in the newly formed connective tissue is of some interest. In the main network of collagen and hyaline it was absent, whilst in the material around the ducts and in the 'masses' of debris it appeared as a rather diffusely staining network made up of intermingled fragments (*Figs.* 122, 125).

It is somewhat difficult to assess accurately the conditions under which hyaline is deposited after irradiation. In some cases with similar histological appearances and dosage levels, where mastectomy was performed following equal time intervals, dense hyaline deposition was found in one case, whereas it might be minimal in another. It can only be assumed that this represents the variability of repair response on the part of the individual, in the same way that degree of fibrous repair following injury or infection varies from person to person. Well-marked hyaline production was found in patients at all dose levels and its appearances were similar within the dose range studied (2000 r to 4000 r).

In those cases receiving a dosage over 3500 r, where complete cellular disappearance occurred, the



A B

FIG. 123.—A, Macroscopical colour photograph showing connective tissue replacement of a scirrhous carcinoma after irradiation. (× ⅔.) B, Same section as in A, stained by the modification of Mallory's method to show the differential colour in the post-irradiation connective tissue. (× ⅔.)

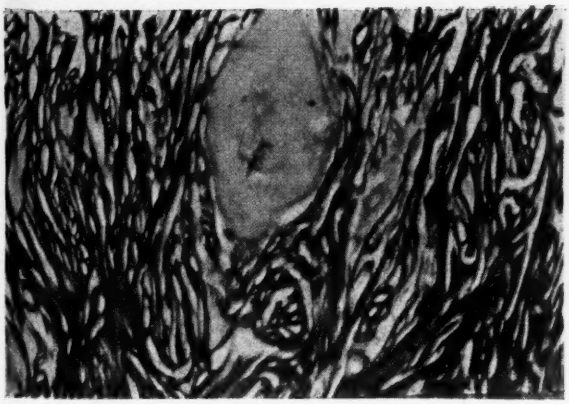


FIG. 124.—'Mass' of connective tissue replacing a malignant area which has remained colourless after staining by the modified Mallory method. (× 360.)

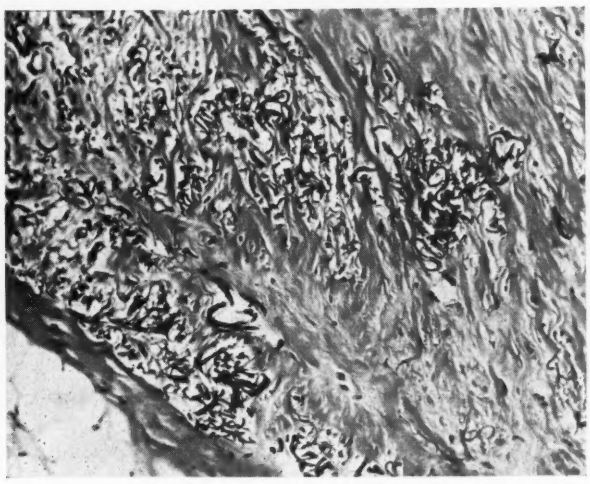


FIG. 125.—Elastic material in an area of tumour destruction (Verhof staining method). (× 120.)

two types of connective-tissue response were well seen, for in some cases the breast after treatment showed such slight connective-tissue increase as to be almost within the bounds of normality (*Fig.* 106), whereas others showed dense hyaline and collagen replacement (*Figs.* 117, 120).

It is suggested that in the former type the majority of cell destruction had occurred by the process of

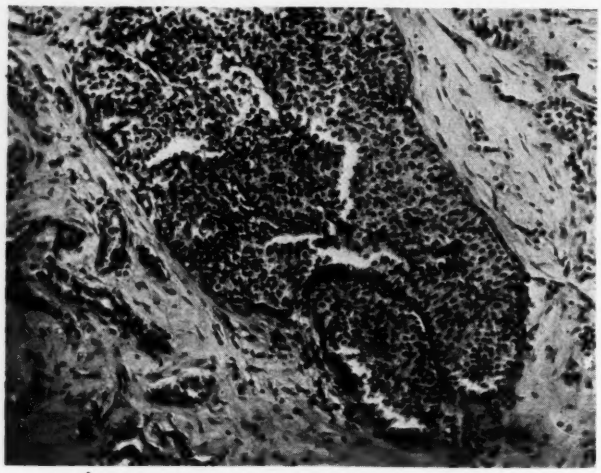


FIG. 126.—Histology before irradiation—tumour largely confined to ducts of uniform cell-type. After 4032 r no malignant cells could be found in the mastectomy specimen. (× 110.)

acute cell dissolution, whereas in the others both cellular degeneration and vascular and connective-tissue change combined in the obliteration of the carcinoma.

DISCUSSION

An outline has been given of the cellular and connective-tissue changes which may occur following irradiation, and an attempt will now be made to correlate the changes found with the dosages given.

It is proposed to analyse these in five groups :—

1. Dosage less than 2000 r.
2. Dosage 2000 r to 2500 r.
3. Dosage 2500 r to 3000 r.
4. Dosage 3000 r to 3500 r.
5. Dosage 3500 r to 4000 r.

Positive findings are considered under the following headings : (*a*) Cell disappearance ; (*b*) Cell change which may be incompatible with further reproduction ; (*c*) Hyaline formation and connective-tissue change.

In this grouping (*a*) and (*c*) are self-explanatory ; (*b*) includes those alterations of cell structure which have been described previously. In assessing these features cases can be placed in the following groups :—

Group 1 : Complete absence of any evidence of malignancy in the specimen examined.

Group 2 : Presence of abnormal malignant cells only, which may be non-viable. In the cases placed in this group only small numbers of isolated cells showing gross degenerative changes were found (*Figs.* 109, 110, 111, and 112).

Group 3 : Some indication of irradiation effect, together with areas of unaltered malignant cells.

Group 4 : No evidence of irradiation change in the specimen examined.

It might be suggested that a case placed in Group 1 may in fact have viable malignant cells in areas of the breast not examined ; therefore it must be repeated that all these cases were subjected to very careful scrutiny, including the examination of 'giant' sections, sometimes cut in several planes.

Based on these findings the following figures are given :—

Dosage	Number of Cases				
	Group 1	*Group* 2	*Group* 3	*Group* 4	*Total*
Less than 2000 r	0	0	1	6	7
2000 r to 2500 r	0	1	5	6	12
2500 r to 3000 r	2	3	7	5	17
3000 r to 3500 r	1	5	7	0	13
3500 r to 4000 r	4	7	0	0	11
					60

Although it is not possible to draw any definite conclusion at this stage, it is difficult to escape certain very suggestive features :—

1. A dosage below 2000 r is insufficient to produce any significant changes, and as the dose is increased a progressively larger number of cases is affected. It is of interest to note that even at the

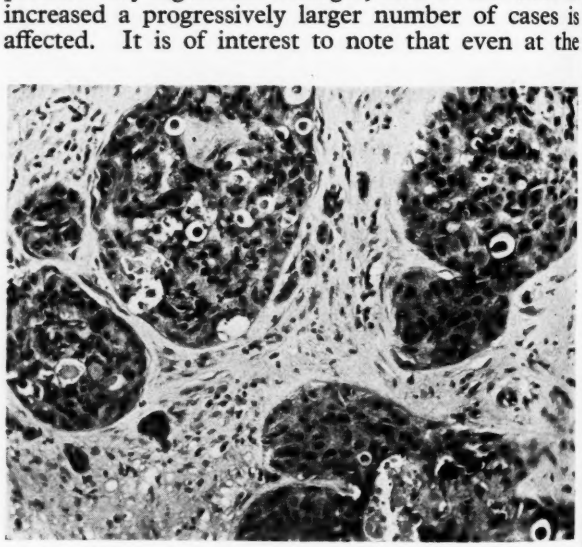


FIG. 127.—Histology before irradiation—tumour with suggestion of 'cribiform' appearance and considerable cell variation. After 3700 r no malignant cells were found in the mastectomy specimen. (× 110.)

lower dose levels some cases are affected sufficiently to be placed in Group 2. It must be assumed that such tumours have a high degree of sensitivity.

2. In all cases receiving a dosage over 3500 r no unaltered malignant cells could be demonstrated (*Figs.* 106, 107). The histology of four examples from this group is shown in *Figs.* 106 B, 126, 127, and 128, demonstrating widely differing histological pictures,

varying from the relatively well-differentiated tumour confined to ducts, shown in *Fig.* 126, to the extremely anaplastic tumour infiltrating widely, shown in *Fig.* 106 B.

It is difficult to escape the conclusion, therefore, that a dosage over 3500 r is coming close to one which confidently might be expected to destroy the majority of breast carcinomata. The damage to normal tissue when the dose is increased above 4000 r with apparatus of the voltage used for this series of cases, is excessive. It would seem, therefore, that the next step is to investigate the results of dosages above 4000 r using super-voltage apparatus where it is possible to localize effects without damaging normal tissues. It is proposed, therefore, to continue along the lines laid down in this paper, observing the changes in carcinoma of the breast following gamma irradiation by means of teleradium therapy and super-voltage apparatus, in order to compare and contrast the results thus obtained with those already set out here.

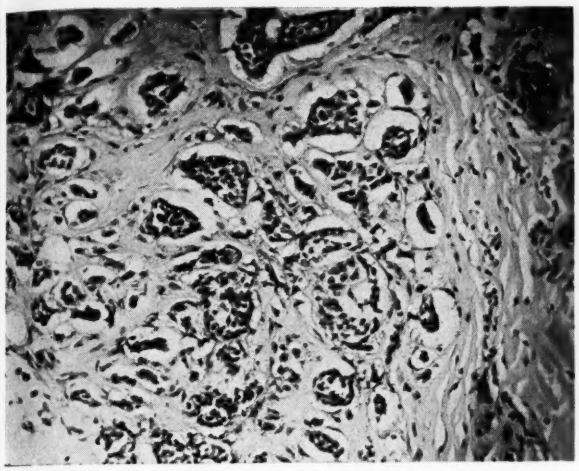


FIG. 128.—Histology before irradiation—scirrhous carcinoma. After 3780 r no malignant cells were found in the mastectomy specimen. (× 110.)

SUMMARY

1. Sixty cases of mammary carcinoma treated with pre-operative high-voltage irradiation are presented.

2. Details of histological changes following irradiation are given.

3. A rough classification of results at varying dosages is suggested.

4. Indications of optimal dosage and further investigations are given.

My grateful thanks are due to Sir Stanford Cade and Professor R. J. V. Pulvertaft for their wholehearted encouragement. I am indebted to the surgical staff of Westminster Hospital and in particular to Mr. E. Stanley Lee, Mr. F. D'Abreu, and Mr. Robert Cox, for the opportunity of investigating the patients under their care. My extreme gratitude is due to Mr. P. G. Hennell and the Directors of the Metal Box Company for the colour photographs of macroscopical specimens, and to Dr. Peter Hansell, of Westminster Hospital photographic department. I should like to point out that without the close co-operation of Dr. F. M. Allchin and Mr. T. M. Prossor, of the Radiotherapy Department of Westminster Hospital, this investigation would have been impossible.

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CARCINOMA OF THE CHEEK IN A CHILD AGED EIGHT YEARS

By E. N. CALLUM, Ashford, Middlesex

The following case-history is reported on account of a number of unusual features.

CASE REPORT

History.—C. B., a boy of 8 years, was first seen on June 17, 1947, with a thin-walled cyst, about the size of a lentil and containing clear fluid, on the inside of the right cheek.

This was considered to be a mucous retention cyst. During an attempt at removal under local anæsthetic the cyst ruptured, with the result that removal was incomplete; unfortunately the specimen was lost.

Fig. 129.—Condition of cheek on September 17, 1947. Duration of illness about three months.

Following operation there was a little local induration, which soon subsided.

On Aug. 13—two months later—the patient was again seen with a swelling in the right cheek, which developed into an abscess containing thick pus; this was incised from inside the mouth ten days later. Subsequent progress was unsatisfactory, with persistence of swelling and pyrexia. Penicillin injections were given from this time (dosage 50,000 units four-hourly, and later on eight-hourly, for a period of 7½ weeks).

On Aug. 28 it was noted that there was an indurated area 1¼ in. in diameter in the right cheek, with central fluctuation under the skin. Two days later an incision was made on the outside of the cheek and much pus liberated. Culture was sterile, possibly because of the penicillin.

Subsequent progress was again unsatisfactory, the wound discharging pus and enlarging, with exuberant growth of granulation tissue.

By Sept. 3 the appearance was highly suggestive of a granuloma and swabs were taken at intervals, more particularly to search for actinomycosis, but with negative results.

On Sept. 17 a biopsy was taken from the summit of the tumour mass, portions being selected for microscopy, for culture, and for guinea-pig inoculation. The only positive finding was some diphtheroid bacilli on culture.

The Wassermann reaction and Kahn test were negative, and white count and X-ray were normal.

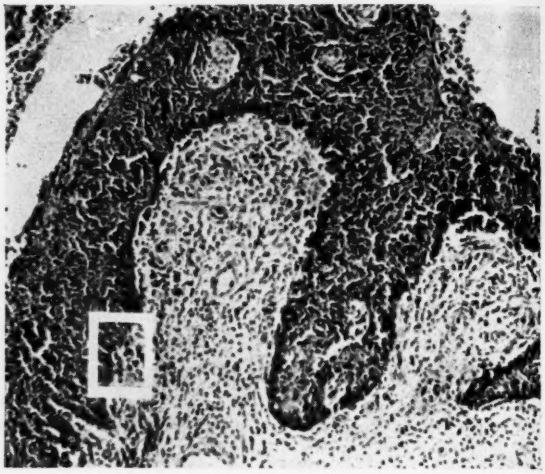

Fig. 130.—Proliferating epithelium covering granulation tissue, acutely inflamed. (× 80.)

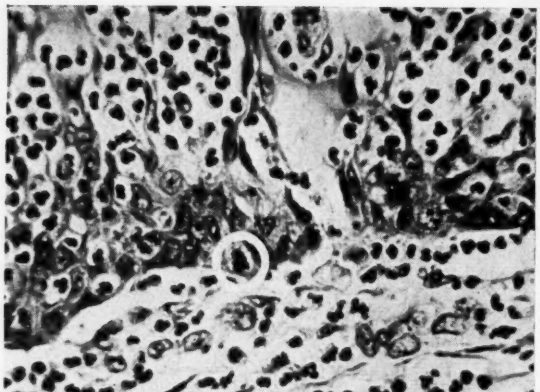

Fig. 131.—Edge of epithelium showing marked polymorphonuclear infiltration of the tissues. The basal layer is intact. A mitotic figure is shown in the circle (area shown in rectangle in *Fig.* 130). (× 335.)

Treatment, in addition to penicillin, consisted of antidiphtheric serum (as a precaution), potassium iodide and N.A.B., all with no effect. *Fig.* 129 shows the lesion at this time. The biopsy report reads as follows: "Sections show a granuloma with many acute inflammatory cells, the cause of which is not apparent. There is no evidence of malignancy or other specific process". (*Figs.* 130, 131.)

On Sept. 29 the lesion had enlarged still more, with a diameter of 3·5 cm. and a depth of 1·5 cm., and a cauliflower appearance very suggestive of malignancy.

A biopsy was taken from the growing edge of the lesion, but the pathological report was inconclusive.

Another picture is shown of the lesion on Oct. 1 (*Fig.* 132).

The patient was seen subsequently by Dr. Parkes Weber, who suggested removal of the bulk of the mass, followed by irradiation.

Accordingly, on Oct. 8 the bulk of the mass was removed with comparative ease, as there was a stratum of necrotic tissue at its base. The raw area, which was 4 cm. in diameter, was carbolized. Biopsy report of this specimen reads as follows: "Sections show normal epidermis merging into an epidermis which is acanthotic, becoming continuous with the tumour mass. The capillaries in the corium are dilated but tend to be empty of blood and there is increased fibrosis which is sparsely infiltrated by inflammatory cells.

"The tumour mass is made up of œdematous epidermoid cells in sheets and columns intimately mixed with acute inflammatory cells (nearly all neutrophil polymorphs with a few eosinophils) and separated by vascular fibrous tissue heavily infiltrated with polymorphs and moderate numbers of macrophages containing broken-down inflammatory cells.

"In most places the epidermoid cells are differentiated and arranged in layers as in normal skin, but are split up by œdema and are very necrotic, especially the prickle cells. The mitotic figures are plentiful, but appear typical. The appearances are those of a granuloma—aetiology not apparent". (*Fig.* 134.)

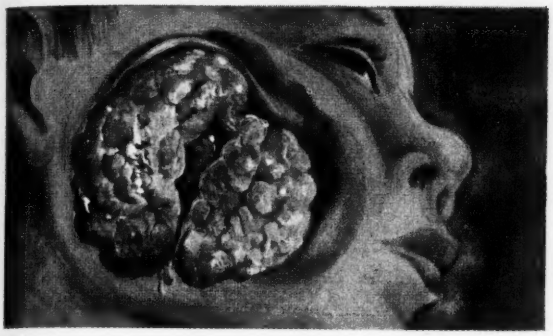

FIG. 132.—Condition on October 1, 1947. Duration of illness about 3½ months.

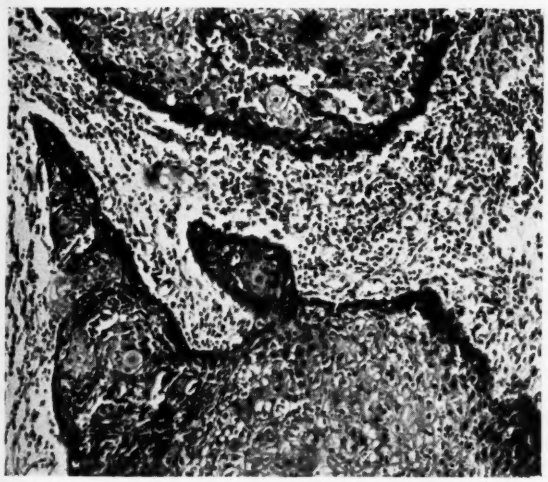

FIG. 134.—Acute inflammation and œdema of all layers. (× 80.)

Irradiation was commenced under the care of Professor Windeyer on Oct. 13 and the first course completed by Nov. 6, eight treatments being given in one area in twenty-four days.

Subsequent progress was satisfactory to a point and on Oct. 21 there was an area of clean granulation only 1 in. in diameter. General health remained good and the granulating surface became smaller and remained clean and free from excessive proliferation. (*Fig.* 133.) By Nov. 24 the granular area was only ½ in. in diameter.

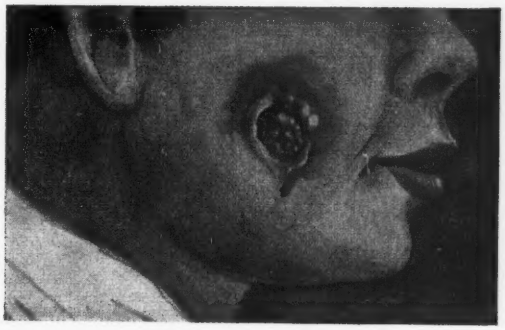

FIG. 133.—Condition on November 24, 1947, after first course of irradiation following excision of tumour mass.

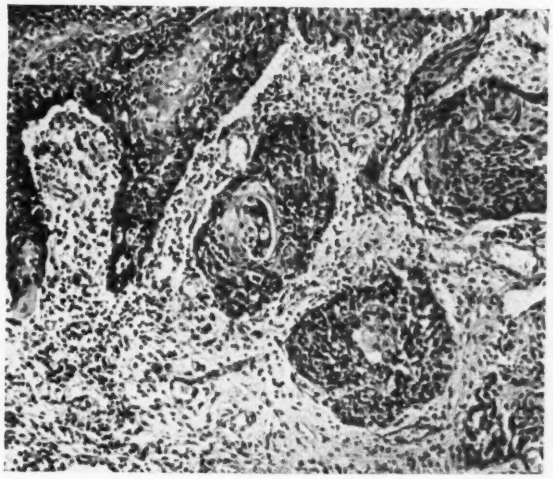

FIG. 135.—Cell nests have now appeared. (× 80).

A further course of irradiation was given between Dec. 17, 1947, and Jan. 20, 1948, six treatments in one area in thirty-five days. The general health remained excellent and only a small unhealthy area remained with a fair amount of underlying fibrosis.

On Feb. 25, 1948, the patient was re-admitted with recommencing proliferation of tissue. There were exuberant granulations about ¾ in. across, with a large, hard, fibrous plaque on the inner side of the cheek.

Biopsy was taken and the report reads as follows: "Sections show that the appearance is very much as it was in previous sections. The material consists of granulation tissue showing much infiltration by inflammatory cells and in which groups of epithelial cells are scattered. These groups show fairly frequent mitoses and in many of the groups the cells are rather spindle-shaped. The surface epithelium is œdematous. Degenerative changes are frequent. While the probability would seem to be that this is a granuloma, I would not like to exclude the possibility that it is an epithelial

tumour and malignant". (*Figs.* 135, 136.) After further deliberation a verbal opinion was given that the condition was a squamous-celled carcinoma.

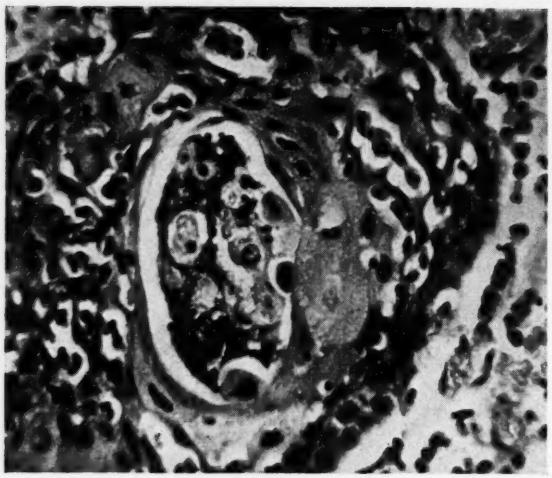

FIG. 136.—Cell nest infiltrated with acute inflammatory cells. (× 335.)

On April 13 a further course of irradiation was considered but was not given.

The condition steadily became worse and the patient was again admitted on July 21, in an obviously hopeless condition. There was a large hard swelling of the right side of the face with an unhealthy necrotic ulcer half an inch in diameter at its centre, and a considerable amount of brawny œdema around.

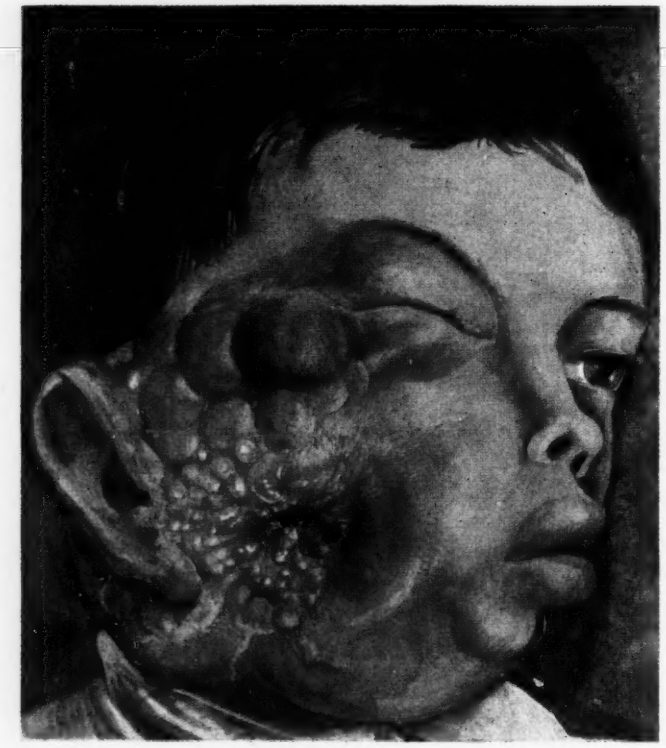

FIG. 137.—Condition on August 10, 1948, shortly before death.

Subsequent progress of the disease was rapid and unrelenting, the œdema increasing so much that the right eye was completely closed and the left eye nearly so, and the whole face grossly distorted.

There appeared to be fluctuation, but only blood-stained fluid was obtained on aspiration.

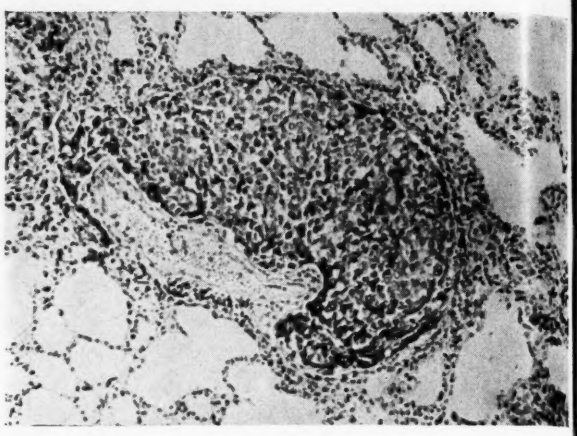

FIG. 138.—Perivascular lymphatic in lung permeated by growth. (× 80.)

By Aug. 10, hard nodules began to appear around the periphery of the main mass and these increased rapidly in number and size (*Fig.* 137).

It was quite obvious by now that the lesion was an extremely rapidly growing and malignant tumour.

The child's condition deteriorated rapidly and on Sept. 8 he became comatose and died a few hours later.

The AUTOPSY REPORT reads as follows: "*Externally.* There was a large fungating growth of the right cheek with a large ulcerated area in the middle. The tumour extended from above the level of the eyebrow to well below the angle of the mandible and from almost the midline of the lip to a point well behind the auricle. At the periphery of the large mass were numerous small nodules of growth, firm and up to a centimeter in diameter. The growth had eroded the wall of the maxillary antrum and invaded the antrum; when inspected from inside the mouth, only a relatively small area of the buccal mucosa was involved.

"On dissection of the *neck* and *axillæ* numerous enlarged and soft lymph-nodes were found; it was difficult to be certain from their appearance whether they were involved in the growth or only enlarged from sepsis. These were found on both sides of the neck, but only in the right axilla. The œsophagus and air passages were normal.

"*Thorax*: There was no free fluid in either pleural cavity and no adhesions; no secondaries could be seen on the surface. On section of the lungs into thin slices five small metastases were found scattered in the periphery. Hilar glands were enlarged. Otherwise the lungs were completely normal. There was no evidence of bronchopneumonia and merely a little hypostasis in the posterior part of the lungs.

"*Heart*: There were no metastases and the pericardium, endocardium, and valves were all normal. The heart muscle showed no obvious change.

"*Abdomen*: All the organs were cut into thin sections. No metastases were found and all the abdominal organs appeared completely healthy.

"*Skull*: The growth had invaded the cranial cavity. There was a mass of tumour occupying the medial wall and extending on to the floor of the middle fossa and occupying most of the floor to a depth of about 2 cm. The bone under the growth in the floor of the fossa was intact, but the bone between the middle fossa and the

nasal sinuses was eroded and the growth had apparently extended into the fossa through the medial wall and spread on to the floor. In the posterior fossa there were two minute masses of tumour which had invaded along the hypoglossal nerve. The pia-arachnoid membrane was intact and there was no invasion of metastasis of the brain."

Microscopical sections showed the presence of squamous-celled carcinoma in cervical glands and in the nodules in the lungs (*Fig.* 138).

Conclusion.—An unusual tumour in the face of a child is described which at first appeared to be inflammatory or granulomatous but was proved to be malignant towards the end of the illness. The growth of the tumour was followed from the very outset to its tragic end, and it was only towards the end that evidence of malignancy was overwhelming.

Acknowledgements are due to many of my colleagues who have given valuable advice, and particularly to Doctors G. Signy, W. F. Hamilton, and C. F. Ross, who have reported on the pathological material.

I am indebted to Miss Nicholson for the excellent drawings and to Mr. E. Targett, F.I.M.L.T., for the equally good photomicrographs.

THE COLLATERAL CIRCULATION TO THE LUNGS

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SINCE Blalock and Taussig conceived their operation whereby patients with Fallot's tetralogy could be improved, and their lives made bearable, by directing a fresh systemic blood-supply into the pulmonary arterial bed, renewed interest in this problem has been aroused. Pott's operation, and Brock's work on valvulotomy, have been the direct outcome of their pioneer work. The essential object of these operations has been to bring a fresh systemic blood-supply to lungs the pulmonary arteries of which are stenosed, and thus to improve the oxygenation of the blood as a whole.

In patients with Fallot's tetralogy, Nature has already made strenuous efforts towards this end. Usually, all around the hilum of the lung, masses of dilated tortuous vessels are found, bringing blood towards the lung roots. These are enlarged collateral vessels endeavouring to bring a fresh systemic blood-supply into the lung.

Barrett (Barrett and Daley, 1949) operated upon a child with Fallot's tetralogy, intending to do a Blalock's operation. However, after a long dissection of the lung root and superior mediastinum had been carried out, it was found impossible to do this for anatomical reasons. The thorax was therefore closed without anything further being done. To everyone's surprise this child recovered and when seen three months later had improved considerably. She was less cyanosed, had ceased squatting, and had an improved exercise tolerance. It was concluded that in the extensive area of dissection, adhesions had developed between the lung and the chest wall and that anastomotic blood-vessels had formed in these adhesions bringing a new systemic blood-supply to the lung. Thus, the original object of the operation had been achieved after all, but by a different method and route from that originally intended. Barrett then devised an operation specifically to create adhesions between the chest wall and the lung, in which collateral vessels could develop. It consisted of stripping and removing parts of the mediastinal and parietal pleura and allowing the lung to come into contact with and adhere to these bare areas. This operation could be used in cases in which for anatomical or other reasons the Blalock-Taussig or Pott's procedure was impossible or inadvisable. A preliminary report of the results of this operation in 6 cases of congenital heart disease with cyanosis has already appeared (Barrett and Daley, 1949) and the results were encouraging. Since this report was written the patients have been kept under observation, and their clinical condition has continued to improve.

It was thought desirable to follow these clinical observations by an experimental investigation. The questions we set ourselves to answer by experiment were :—

1. Does a lung, whose main supply of blood (via the pulmonary artery) has been curtailed or cut off, attract to itself a collateral circulation?

2. If so, where does this collateral circulation come from, how does it enter the lung, and how, if at all, does it anastomose with the pulmonary arterial system in the lung?

3. Does the creation of adhesions, as in Barrett's operation, supply an extra collateral circulation to such a lung, and if so, how do these vessels enter the lung and how do they anastomose?

4. Is a lung, whose main blood-supply comes through collateral channels, an efficient respiratory organ? Can it support life?

Before passing on to an account of our experiments and results, a brief review of previous work in this field and the present state of our knowledge of the bronchial circulation must be given.

REVIEW OF PREVIOUS WORK

The bronchial arteries were first described as a separate blood-supply to the lung by de Marchetti in 1654. Wide differences in the origin and distribution of these arteries have since been observed in different species. In man, and in the dog, they arise from the aorta and/or the intercostals. W. S. Miller

(1937), between the years 1900 and 1925, worked out the detailed anatomy of the intrapulmonary distribution of the bronchial arteries. He concluded that these arteries supply the bronchial tree as far as the small bronchioles. They also give branches to the subpleural capillary network on the surface of the lung. He showed that the bronchial arteries supply the vasa vasorum to the larger pulmonary arteries, and pointed out that these might be mistaken for anastomosing vessels. Ghoreyeb and Karsner (1913) and Berry and Daly (1932) showed by injection and perfusion experiments that there could be an interchange of blood between the bronchial and pulmonary systems depending largely on the relative pressure. In 1931 Berry, Brailsford, and Daly stated that the available evidence favoured the opinion that in man and the dog the capillaries are the only means of communication between the two systems. It was not until the important paper by Holman, Mathes, and Reichert appeared in 1932 that doubt was thrown on this statement. Their experiments led them to postulate a proximal shunt between large bronchial arteries and large pulmonary arteries. They found that shortly after ligature of the pulmonary artery to a lobe, they were able to inject the whole of the pulmonary vascular tree with radio-opaque material via the bronchial artery. This was not possible in a normal lung. The same result could be obtained to a slightly lesser extent in a lobe which had been collapsed by occlusion of its bronchus. This idea of a " broncho-pulmonary shunt " is very important in many pathological conditions of the lung, and particularly in the development of its collateral circulation. We shall present, later in this paper, evidence to support the existence of this shunt.

Virchow (1847, 1851, 1856) first observed that following occlusion of a pulmonary artery, a collateral circulation developed to that lobe via enlarged bronchial and intercostal arteries. Schlaepfer (1924, 1926) showed that following ligature of the main pulmonary artery to the lung, an increased bronchial supply through dilated bronchial arteries occurs. Within the last year, Bloomer, Harrison, Lindskog and Liebow (1949) have studied the respiratory function and blood-flow in the bronchial arteries, after ligation of the pulmonary arteries, in dogs. By application of Fick's principle to data obtained by bronchospirometry, and analysis of the systemic arterial blood, the extent of the collateral circulation to the lung was estimated. Most of the increase in blood-flow occurs within the first two weeks after tying the pulmonary artery, but is slowly progressive for at least eighteen months. This collateral circulation may then exceed in volume one-third of the normal output of the right ventricle, and is a burden entirely on the left side of the heart. They also state that " The collateral bronchial circulation of the left lung is insufficient to support life for more than a few minutes, even twenty-one months after ligation of the pulmonary artery ".

These same workers have shown, by bronchovascular corrosion casts (using Vinylite) in human operation specimens of bronchiectatic lungs, a great expansion of the *bronchial* vascular bed, and they have demonstrated the existence of pre-capillary anastomoses between bronchial and pulmonary arteries, some of which are of quite large size (exceeding 50 μ in diameter).

EXPERIMENTAL WORK

Procedure.—Dogs were used as experimental animals, because experience has shown that their anatomical and physiological make-up is similar to that of man. The main pulmonary artery to one lung was tied at the first operation. (The left pulmonary artery was found easier to approach than the right, so this was used in our later experiments.) This procedure, we argued, would produce conditions in the lung comparable to those obtaining in the case of congenital pulmonary stenosis. About three months were allowed to elapse, and then the same side of the chest was reopened. A thorough inspection of any collateral circulations which had developed

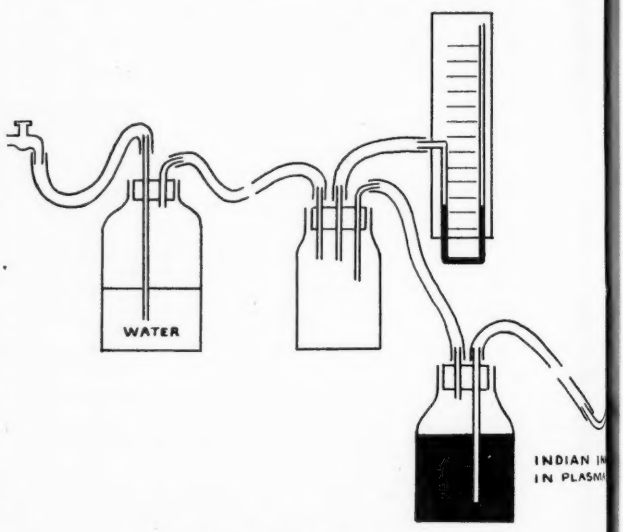

FIG. 139.—Apparatus used for injection.

during that time was made. Then as much as possible of the parietal and mediastinal pleura was stripped and the chest closed again. A further three months were allowed to elapse, to allow time for a collateral circulation in the adhesions to develop. Then the dogs were investigated by the following two methods :—

1. Under anæsthesia the side of the chest opposite to that on which we had previously tied the pulmonary artery and created adhesions was opened. The main bronchus to that lung was isolated and tied off with a piece of tape, and the chest rapidly closed. These animals had had one main pulmonary artery tied and the opposite main bronchus tied. Therefore life depended entirely on the collateral circulation via the bronchial arteries and adhesions to the one lung which was being ventilated. This was one means of demonstrating the efficiency of the new collateral blood-supply to a lung.

2. Immediately after death the lung was injected with an indian ink injection mass, either via the bronchial arteries only, or via the adhesions only, or both. The advantages of this method were twofold. First, the course taken by the injection could be followed by the naked eye and one could see quite easily whether the adhesions and lung could

be injected from the chest wall by the fact that they turned black. Second, once the injection was finished a specimen could be fixed and frozen sections cut, thus giving a more detailed picture of the vascular channels involved.

Technique.—The injection used was 5 per cent indian ink suspended in plasma. With the aid of the simple apparatus shown in *Fig.* 139, the injection could be given at any desired pressure. We usually started the injection at a pressure of about 60 mm. Hg and ended with a pressure of 100 mm. Hg.

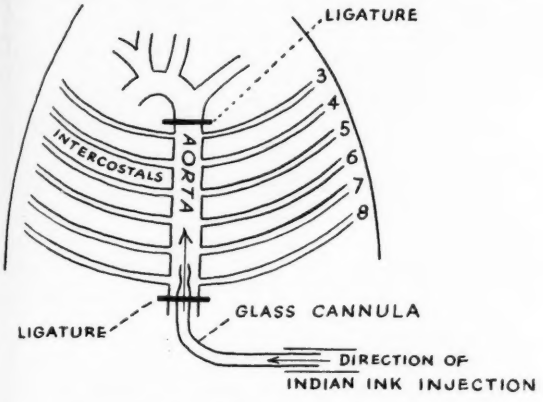

FIG. 140.—Diagram showing injection pathway.

These pressures are not higher than a dog's normal arterial blood-pressure, so the possibility of artefact being produced by an injection at too high a pressure can be excluded.

The dogs were prepared for the injection by the following method: The chest and abdomen were opened by a long midline sternum-splitting incision. The aorta was isolated and ligatured just distal to the left subclavian artery. The injection cannula was tied into the aorta, pointing upwards (i.e., against the normal blood-stream) at about the level of the 7th or 8th intercostal vessels. An injection given under these conditions injects the aorta and all its branches between the origin of the 3rd or 4th intercostal vessels and the 7th or 8th intercostal vessels (these include the bronchial arteries, and the arteries to the pericardium and œsophagus). To exclude the bronchial arteries and inject the lung entirely from the chest wall adhesions it was only necessary to place a ligature around the lung root, divide it completely and let the lung collapse on to the chest wall, held only by its adhesions. Under such conditions indian ink injected into the aorta can only enter the lung through the adhesions. Reference to *Figs.* 140 and 141 will make this clear.

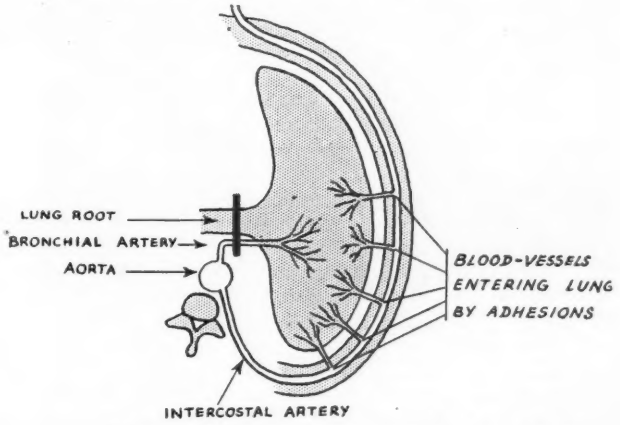

FIG. 141.—Diagrammatic cross-section of dog's chest illustrating mode of entry of the bronchial vessels and of the vessels in the adhesions: the bar represents the site of division of the lung root which limited the perfusion to the anastomotic vessels, as described in text.

DESCRIPTION OF EXPERIMENTS

Five dogs were used in the experiments. The first one was dissected in order to gain a knowledge of the anatomy of the lung root and bronchial arteries of a dog. The second animal was sacrificed to try out our injection technique and to provide a control specimen of normal lung injected through the bronchial arteries (*Fig.* 142). A satisfactory injection of both lungs was obtained. In two of the sections of these lungs we discovered a small branch of a bronchial vessel (densely injected with black) entering a large pulmonary artery (*Figs.* 143, 144).

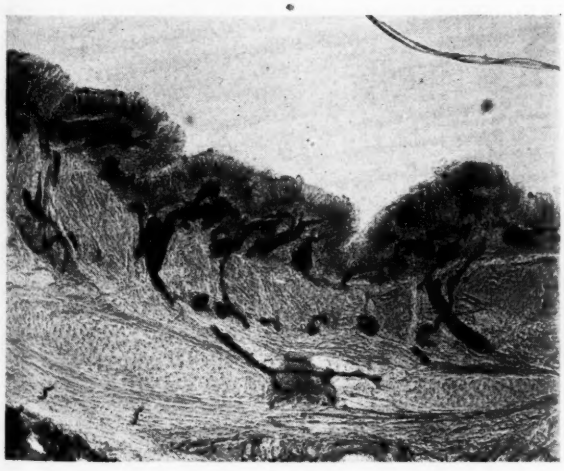

FIG. 142.—*Dog* 2. Normal dog's lung. Injected via bronchial arteries. Showing injection of the bronchial arteries in the wall of a large bronchus (cf. *Fig.* 148). (× ½.)

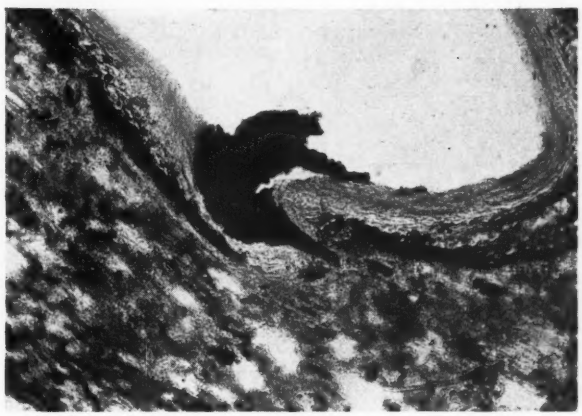

FIG. 143.—*Dog.* 2. Normal dog's lung. Injected via bronchial arteries. Shows an anastomosis between bronchial system and one of the larger pulmonary arteries. Note that the large pulmonary artery itself is uninjected. (× ½.)

These two sections are of interest because they are the first in which precapillary anastomoses between bronchial arteries and pulmonary arteries have been demonstrated in a *normal* lung. It is possible that the opening up and dilatation of these small anastomoses which already exist provides the channels for the bronchopulmonary shunt which we found to occur in our experiments.

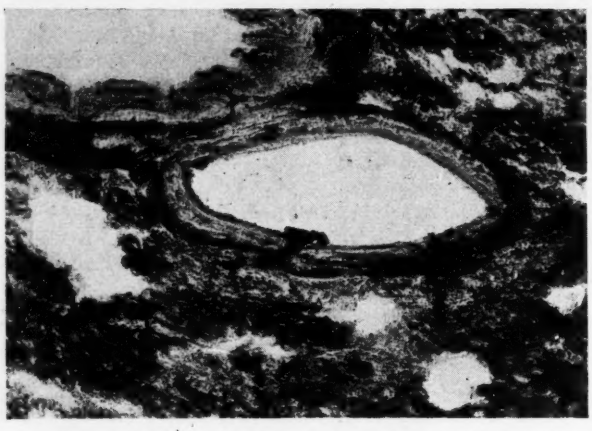

FIG. 144.—*Dog* 2. Normal dog's lung. Injected via bronchial arteries. Shows an anastomosis between bronchial arterial system and a large pulmonary artery. Note that the large pulmonary artery itself is *uninjected* and that the lung capillaries are uninjected (cf. *Figs.* 146 and 147). (× ⅛.)

Dog 3.—

FIRST OPERATION (November, 1948).—Through a right thoracotomy the azygos vein was divided between ligatures, and a large pulmonary artery, thought at that time to be the main right pulmonary artery, was tied. The thorax was closed and the dog made an excellent recovery.

FIG. 146.—*Dog* 3. (Pulmonary artery tied six months ago, adhesions made three months ago): Upper lobe right lung. Injected entirely through the adhesions. *Note*: (1) Capillaries of the lung are *well* injected; (2) Large pulmonary artery branch is also full of injection material. (× ⅛.)

SECOND OPERATION (March, 1949).—A right thoracotomy through a slightly lower incision than the last one was done. It was at once apparent that the vessel which had been tied was not the main pulmonary artery, but the branch to the upper lobe. The upper lobe was fully expanded but paler in colour than the lower lobes, which were normal pink. A mass of tortuous dilated vessels coursed towards the hilum of the upper lobe. A pleural strip operation was then performed.

THIRD OPERATION (July, 1949).—The dog was given an overdose of nembutal and the thoracic cavities were inspected through a long midline sternal split incision. The appearance was as at the second operation in March with the addition of two things :—

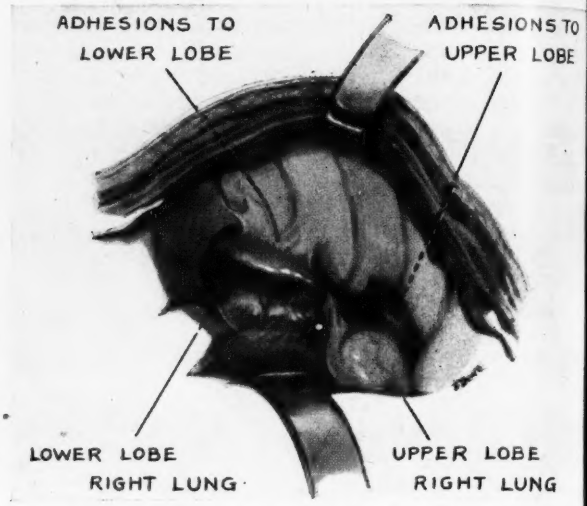

FIG. 145.—*Dog* 3. Notice that the upper lobe of the lung, which has had its pulmonary artery occluded, is paler in colour than the lower lobe, that it has vessels coursing over its surface, and that the adhesions to it have been densely injected. The adhesions to the normal lower lobe are avascular.

FIG. 147.—*Dog* 3. (Pulmonary artery tied six months ago, adhesions made three months ago): Upper lobe, right lung. Injected entirely through the adhesions. *Note*: (1) Dense injection of lung capillaries; (2) Small branch of pulmonary artery accompanying bronchus is full of injection material. (× ⅛.)

1. Many new adhesions were present, particularly in the paravertebral gutter and underlying the two incisions, to both the upper and the lower lobes.

2. The adhesions to the upper lobe were noticeably more vascular than those to the lower lobe, and the whole surface of the upper lobe was covered by a fine network

of vessels. These were a new development, not visible at the previous operation.

The dog was then prepared for injection in such a way that the upper and lower lobes could be injected via the adhesions only (i.e., a ligature was placed around the hilum of the whole of the right lung). The result of this injection was very striking. In less than a minute the adhesions to the upper lobe turned black, and the fluid could easily be seen entering the numerous small new vessels branching over the surface of the lung. The adhesions to the lower lobe remained uninjected. This contrasting appearance between the adhesions to the upper and those to the lower lobes was so striking that an artist was summoned and a drawing made on the spot (*Fig.* 145). Microscopy of the lung later confirmed that the vascular bed of the upper lobe had been thoroughly injected from the adhesions, whereas the lower lobes were uninjected. (*Figs.* 146, 147).

Dog 4.—

First Operation (December, 1948).—Left thoracotomy. The left main pulmonary artery was isolated and tied. Good recovery.

Second Operation (March, 1949).—The left chest was opened again, a little below the original thoracotomy incision. The whole of the lung was paler than normal

Fig. 148.—*Dog* 4. (Pulmonary artery tied seven months ago, adhesions created four months ago): Left upper lobe. Injected entirely via the adhesions to the chest wall. Shows injection of bronchial arterial system in the wall of a large bronchus. (× ⅛.)

and there was a mass of tortuous enlarged anastomotic vessels going towards the hilum. A pleural strip operation was then performed and the dog again made an excellent recovery, its activity being in no way affected.

Third Operation (August, 1949).—A *right* thoracotomy incision was made, the azygos vein divided, and the right main bronchus isolated. A trial occlusion of the bronchus with clamps was then done. Respirations rose rapidly from 28 to 40–50 per minute and the pulse-rate to 190–200 per minute. The animal seemed better when the thorax was temporarily closed. After 25 minutes the heart-rate and respiration-rate began to fall and the dog was on the point of death. The clamp was therefore removed, the lung re-expanded, and the dog's state rapidly returned to normal. Twenty minutes were then allowed to elapse to allow complete recovery and the anæsthesia was lightened so that spontaneous respiratory efforts were being made. Then a tape was passed round the right bronchus, and preparations were made to close

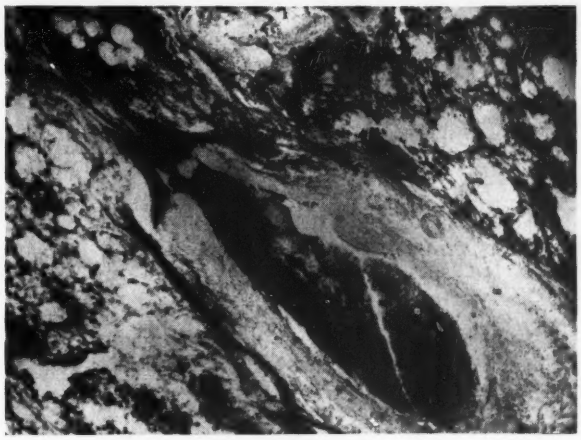

Fig. 149.—*Dog* 4. (Pulmonary artery tied seven months ago, adhesions created four months ago): Left upper lobe. Injected entirely via the adhesions to the chest wall. Shows large pulmonary artery branch, full of injection material. (× ⅛.)

the chest and make it airtight as quickly as possible. The tape was tightened to occlude the right main bronchus, the left lung was fully inflated, and the chest closed quickly (about 2 minutes). The dog was then breathing oxygen through a packed-off intratracheal tube, with spontaneous respiration. As before, the respiration-rate rose rapidly to between 45 and 50 per minute and the pulse to between 190 and 200 per minute. The dog lasted for fully 50 minutes in this steady state, the oxygen cylinder then suddenly failed, and before a new one could be fetched the dog was dead.

The thorax was then opened by the usual long midline incision. It was first confirmed that (*a*) the right lung had collapsed completely and the right main bronchus had been, in fact, occluded; and (*b*) the left main pulmonary artery had been tied and was still occluded. There was a little blood in the right thorax, perhaps 1 oz.

The left thorax was then inspected. The left lung was paler than normal and was covered with masses of small pink tortuous vessels (as in *Dog* 3). Numerous and extensive adhesions were present, particularly in the posterior half of the thorax. All these adhesions were vascular; large blood-vessels running from the chest wall to the lung could be seen with the naked eye. The intercostal vessels in the spaces opposite these adhesions were large and tortuous (much as in human cases of coarctation).

The left and middle lobes adhered firmly to each other and to the chest wall. The hilar pedicle of these two lobes was then ligatured in one and cut across on the lung side of the ligature. This allowed these lobes to collapse on to the chest wall, held in position by their adhesions only. The orifices of the big hilar vessels on the cut surface of this part of the lung could now be observed with ease. The dog was then prepared for injection in the usual way, so that these lobes were being injected through adhesions only.

When the injection was started, we had under observation a large open pulmonary artery, bronchus, and pulmonary vein, grouped together in the cut hilum of the left upper lobe. To our astonishment no sooner had the injection started than black injection fluid began to pour from the open mouth of this pulmonary artery. This was swabbed away by pledgets of cotton-wool

continuously. Then, gradually, after about a minute, the lung itself began to turn black. During the whole period of the injection the injection fluid continued to pour out of the open end of this pulmonary artery.

We regard this observation as important. The fact that fluid gushed out of the pulmonary artery as soon as the injection started, and at least a minute before the lung tissue itself turned black, can mean one thing only—namely, that vessels in the adhesions communicate with relatively large vascular channels in the lung, which in turn anastomose with fairly large pulmonary arteries. These anastomoses must be precapillary in situation, otherwise the lung tissue would have turned black before anything came out of the pulmonary artery. It also indicates that a very large volume of blood can be poured into the lung via the adhesions (microscopy later showed that these "large vascular channels in the lung" were, in fact, the dilated bronchial arteries in the lung). (*Figs.* 148, 149.)

Dog 5.—

FIRST OPERATION (December, 1948).—Left thoracotomy, left main pulmonary artery was tied. The animal made a perfect recovery.

SECOND OPERATION (March, 1949).—A left thoracotomy incision, slightly lower than the previous one, was made. We observed that the lung was slightly paler than normal but no adhesions were present. The usual mass of tortuous anastomotic vessels were running towards the lung root (as in *Dogs* 3 and 4). A pleural strip operation by the usual technique was done, and the chest closed. Again the dog made a perfect recovery.

THIRD OPERATION (September, 1949).—Under closed-circuit ether-oxygen anæsthesia the *right* chest was opened, and with some difficulty the right main bronchus was isolated and tied with a piece of tape. The chest was then rapidly closed and the animal allowed to breathe pure oxygen from the circuit (with spontaneous respiration). In view of our experience with *Dog* 4, we had hoped to show that with oxygen the animal could survive for some hours; but, to our surprise, after only 15 minutes it became evident that the dog was failing. Respirations became slower and shallower, the pulse-rate began to fall and the dog died within 30 minutes. We were at a loss to explain this until on opening the chest to inspect and prepare the dog for injection, the reason was apparent—there were no adhesions at all. In spite of the pleural strip operation 6 months before, not a single adhesion had formed. The pleura had completely re-formed and the sites of the operation and extensive pleural stripping in the paravertebral gutter were shown by white linear shining scars. A possible explanation for this is that the original pleural strip operation had gone off very smoothly, with very little operative trauma and very little loss of blood. Moreover, it is possible that during the immediate post-operative period there may have been a small pneumothorax, keeping the lung out of contact with the newly-scarified chest wall. In any case, this experiment indicates a possible reason for failure in some pleural strip operations and the necessity for good post-operative care.

It was confirmed that the left main pulmonary artery had been tied and remained occluded, and that the right main bronchus had been securely tied. The dog was then prepared for injection and both right and left lungs injected via the bronchial arteries in the usual way.

RESULTS OF STUDY OF THE LUNG SECTIONS

Every injected lung specimen was fixed in alcohol, and frozen serial sections prepared from it. Systematic search through these brought out various other points of interest.

Study of sections of normal lung injected via bronchial arteries showed: (1) A fine injection of the bronchial arterioles; (2) The pulmonary arteries themselves were uninjected; (3) The lung capillaries were uninjected; (4) Careful search revealed several examples of small bronchial vessels entering large pulmonary arteries. (*Figs.* 142, 143, 144, 145 illustrate these points.)

On the other hand, the sections of lung which had had their pulmonary arteries tied showed marked differences. Moreover, they showed the same general microscopical picture whether they were injected via adhesions alone, the bronchial arteries alone, or both together. The following points were noted: (1) The injection of the lung capillaries was very marked. (*See Figs.* 146 and 147, and cf. *Figs.* 143 and 144.) (2) The larger branches of the pulmonary arteries were always full of injection in these cases (*Figs.* 146, 147, and 149, and cf. *Figs.* 143 and 144). (3) The actual bronchial arteries in the lung and in the walls of the large bronchi could be injected quite easily from the adhesions alone (*Fig.* 148).

A study of these sections shows that the bronchial and the pulmonary arterial system and the lung capillaries can be injected through collateral vessels developed in adhesions to these lungs. Moreover, an identical histological picture is seen when these lungs are injected only via the dilated bronchial arteries. We have shown that in normal lung it is impossible to inject either the pulmonary arteries or the lung capillaries with our technique, via the bronchial arteries. The conclusion, therefore, must be as follows: In these lungs, in which the pulmonary artery has been tied off, blood from vessels in the adhesions and from the dilated bronchial vessels enters the pulmonary arterial system in the lung and so gets into the lung capillaries. In other words, a considerable anastomosis between the bronchial arterial system and the pulmonary arterial system within the lung has developed, which we have named the bronchopulmonary shunt.

CONCLUSIONS AND DISCUSSION

Our experiments have thus confirmed much of the previous work in this field. It has been shown once again that after the main pulmonary artery has been tied, a collateral circulation develops through the bronchial arteries, which enlarge greatly and receive tributaries from several intercostal vessels, from the œsophageal plexus, and from the internal mammary and pericardiacophrenic arteries. The work of Holman, Mathes, and Reichert (1930, 1932), who showed that under these conditions the pulmonary artery can be injected from the bronchial arteries, has been confirmed.

We have, then, shown that such a lung can attract to itself, through artificially created adhesions, a profuse new blood-supply, and that these new blood-channels anastomose directly with large branches of the pulmonary artery within the lung. The effectiveness of this new blood-supply to the lung is indicated in the experiment on *Dog* 4, described above. Adhesions created to a normal lung do not become vascular.

Evidence has been presented of the existence in normal lung of small anastomotic channels between

the bronchial arterial system and the larger pulmonary arteries. This small bronchopulmonary shunt mechanism, which is probably non-functional in the normal animal, becomes (we think) enormously dilated after occlusion of the pulmonary artery, allowing large volumes of blood entering the bronchial artery, or through adhesions, to flow straight into the pulmonary arterial system and thence into the lung capillaries.

This shunt mechanism may be of the greatest importance in certain pathological conditions of the lung. Liebow, Hales, and Lindskog (1949, a, b) in America have recently shown that in severe bronchiectasis the bronchial arterial system hypertrophies and develops large communications with the pulmonary arteries. This, after all, is only in line with the physiological needs of diseased tissue, viz., it wants arterial blood for its nutrition, not venous blood. In the same way, a lung which is atelectatic depends for its nutrition on arterial blood, and under such conditions the bronchopulmonary shunt mechanism may again come into action, as was shown by Holman, Mathes, and Reichert. In fact, it would seem that hypertrophy and dilatation of the bronchial arteries and opening up of the shunt may be a fundamental mechanism in the nutrition of any large diseased area of lung, whether it be collapse, consolidation, tuberculosis, or infection. It may explain why the large quantities of blood expectorated in hæmoptyses in tuberculous and in bronchiectatic patients are always bright red in colour, not venous.

There is another possible result of this shunt. The systemic arterial pressure is over 100 mm. Hg, the pulmonary arterial pressure is about 40 mm. Hg. If the bronchopulmonary shunt is opened up under disease conditions, then the pressure in the pulmonary arteries must rise; i.e., pulmonary hypertension must result. Liebow and his associates have recently shown that the pressure in the pulmonary artery on the diseased side in a patient with gross bronchiectasis is, in fact, higher than that on the normal side. Also oxygen content of the blood in the pulmonary artery on the diseased side is higher, giving confirmatory evidence to this theory.

Lastly, it remains to be demonstrated whether or not this bronchopulmonary shunt is a means of nutrition of the fœtal lung.

SUMMARY

1. A lung whose pulmonary artery has been occluded will attract to itself a large collateral blood-supply via artificially created adhesions.

2. Evidence is presented for the existence in the normal lung of small precapillary anastomoses between the bronchial and the pulmonary arterial systems.

3. Blood from the collateral vessels enters the pulmonary arteries (and hence gets into the lung capillaries) by means of precapillary anastomoses between the bronchial arteries and the pulmonary arteries within the lung.

4. This mechanism for supplying systemic arterial blood to the lung capillaries has been called the 'bronchopulmonary shunt'.

5. The possible importance of this shunt in the physiology and pathology of the lung is discussed.

Our thanks are due to Miss K. M. Murray and Mr. D. N. Barran for giving the anæsthetics; to Mr. D. P. King for the sections, and especially to Professor D. V. Davies for his continued interest and help throughout this work.

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CHEWING-GUM VESICAL CALCULUS IN THE MALE

BY THOMAS MOORE, MANCHESTER

THE number and varieties of foreign bodies which have from time to time been found in the bladder surpass the imagination. In the female, the short and wide urethra accounts for the many types which are intentionally or accidentally introduced by this route. The male urethra, however, is a tortuous channel of varying diameter, about 8 in. long. It would not be expected to present a facile route for the introduction of any foreign body. In fact, the technique of its negotiation by a sound is, to the beginner, difficult to learn. It is beyond comprehension that a piece of chewing gum can be introduced along it by an unskilled male patient. Truth is indeed stranger than fiction.

The method is that the gum is rolled into a pencil-like structure and inserted by the patient for the purpose of producing an orgasm by stimulation of the deep urethra. During the act, the deep part of the gum breaks off and, by the successive contractions and relaxations of the perineal muscles,

is sucked into the bladder. The practice is probably more common than is realized. It only comes to light in those cases in which the gum breaks, and then only some time later when symptoms supervene. The gum, being inert, causes relatively little trouble at first, but when infection or phosphatic incrustation occurs, symptoms of cystitis appear. Patients are reluctant to confess to the practice, so that the time between the insertion of the gum and the onset of symptoms is difficult to determine. In 1937, MacKenzie reported a case and could find only 5 others in the literature. I have been unable to find any further cases, but wish to report 2 which I have treated.

CASE REPORTS

Case 1.—Private D. D., aged 23 years. An American soldier.

The patient was first seen on Dec. 3, 1942. For six weeks he had complained of great frequency of micturition and occasional hæmaturia. He had had prolonged treatment with sulphapyridine elsewhere and the symptoms had decreased in severity but had not entirely disappeared.

On Examination.—The patient's general condition was good. No abnormality was found in the abdomen or external genitalia. Rectal examination was normal. The urine contained numerous W.B.C. and, on culture, grew Gram-positive cocci and diphtheroids. Cystoscopy under local anæsthesia showed some basal cystitis and, lying at the base of the bladder, a worm-like structure about 4 cm. long, with a diameter of 0·5 cm.

At Operation.—On Dec. 9, under general anæsthesia, the bladder was exposed and opened through a midline incision and the stone removed. The bladder and

Fig. 150.—*Case* 1. The stone on removal.

wound were closed and the bladder drained by an inlying urethral catheter.

The patient had an uninterrupted convalescence and was discharged to the convalescent home seven days later. The wound was healing satisfactorily and he was passing urine normally.

Pathology.—The stone was a worm-like structure with a diameter of 5 mm. and curled into the curious shape shown (*Fig.* 150). Its surface was smooth and of a dark-brown colour, streaked with areas of light brown. In consistency it resembled dry, firm putty. Cross-section showed that it consisted mainly of a central core of a dirty-grey substance with a thin covering of dark-brown material. Chemical examination showed that the central core gave all the reactions of chewing gum and the outer coat consisted of mixed phosphates and oxalate.

Case 2.—Sergeant S. A., aged 26 years.

The patient was seen on Jan. 7, 1944, having been referred from another hospital for a urological opinion. The history was that about October, 1943, he noticed a burning in the perineum on passing urine and developed great frequency of micturition both day and night. He had had about three months' treatment in another hospital, including courses of sulphapyridine, sulphanilamide, and mandelic acid without complete resolution of the symptoms.

On Examination.—The patient's general condition was good. The abdomen and external genitalia were normal and rectal examination showed no abnormality.

Fig. 151.—*Case* 2. The stone.

The urine contained a few W.B.C. Cystoscopy under local anæsthesia showed a worm-like calculus with a diameter of about 0·5 cm., arranged in the shape of a ring about 2·5 cm. in diameter. It was recognized as a chewing-gum calculus, but the patient denied all knowledge of any chewing gum getting into his bladder. Plain radiographs and intravenous urograms showed no abnormality.

At Operation.—On Jan. 16, 1944, under general anæsthesia, the bladder was exposed and opened through a midline suprapubic incision and the stone removed. The bladder and wound were closed and the bladder drained by an inlying urethral catheter.

The patient made slow progress owing to continual blocking of the catheter, but was eventually discharged three weeks later, when he was passing urine normally.

Pathology.—The stone was a cylindrical structure with a diameter of 4 mm. arranged in the shape of a ring (*Fig.* 151). It was quite hard and had a granular, light-brown surface. On section it was seen to have a soft dirty-grey core covered by a shell of a brittle light-brown substance. Chemical examination showed that the central core gave all the reactions of chewing gum and the outer covering consisted of mixed phosphates with a little oxalate.

The first patient continually denied ever having introduced any chewing gum into the urethra. The second did so at first, but immediately before the operation told me confidentially that he had introduced the gum.

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THE MORPHOLOGY OF THE BRANCHIAL GLOMERA AND THEIR TUMOURS, WITH A REPORT OF A CASE OF AORTICO-PULMONARY GLOMUS TUMOUR

By R. S. MONRO
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THE existence of the carotid body was discovered by von Haller in 1743. Its tumours remained unrecognized until Marchand's original description in 1891. Until comparatively recently the existence of similar glandular structures in the superior mediastinum in relation to the great vessels has passed unnoticed, and hitherto tumours arising from these organs in man have not been described.

From all aspects the case which is here presented is unusual, and it may be unique, for it is believed to be the first account of a tumour arising from an aortico-pulmonary glomus in man.

MORPHOLOGY OF THE BRANCHIAL GLOMERA

The morphology of the carotid body and the anatomy of its homologues are not widely known, but are most pertinent to the correct interpretation of this case. Luschka (1862) gave the first histological description of the carotid body, and postulated its derivation from pharyngeal entoderm after the fashion of the parathyroids. He also commented on the histological resemblance between the carotid body and the adrenal medulla, a point later emphasized by Kohn (1900), who stressed the occurrence of apparent chromaffinity in carotid body tumours, postulated a neural origin, and adumbrated the paraganglionic theory to which Zuckerkandl (1912) added the finishing touches. The paraganglionic theory, in so far as it concerns the carotid body, has not, however, stood the test of time, but has been discredited by more detailed histochemical investigation and more exhaustive embryological research. In connexion with this last, Boyd (1937), examining very early human embryos, has demonstrated that the principal cells of the human carotid body derive as a thickening of the media of the internal carotid immediately above the bifurcation, that is, from that part of the vessel which represents the commencement of the third branchial arch artery. The appearance of neural tissue in this vascular thickening, by migration along the glossopharyngeal nerve, is a later and subsidiary phenomenon.

The significance of the situation and peculiar derivation of the carotid body is more readily comprehensible now that its function is more fully understood. The related carotid sinus is concerned with the maintenance of a constant circulation, inducing cardiac inhibition when an undue rise in general blood-pressure occurs, and acceleration with a fall. The carotid body, on the other hand, is concerned with the maintenance of a constant chemical constitution of the blood, modifying respiratory activity in response to oxygen lack, or carbon-dioxide excess (Dripps and Comroe, 1944). The carotid body is an organ of considerable morphological antiquity, and, as a structure intimately concerned with respiratory exchanges, it is not surprising to find that in primitive vertebrates this controlling mechanism is derived from and related to the vessels supplying the gill clefts. It is no more surprising that the human embryo, in the recapitulation of its phylogenetic history, derives this organ, which still retains its influence on respiratory function, from the ontogenetic equivalent of the third branchial arch artery, whilst the development of

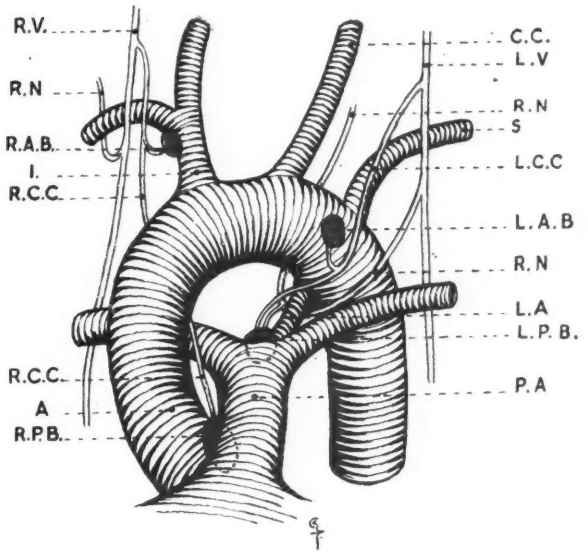

FIG. 152.—Diagram of the aortico-pulmonary glomera in relation to the great vessels. C.C, Common carotid artery; S, Subclavian artery; I, Innominate artery; A, Aorta; P.A, Pulmonary artery; L.A, Ligamentum arteriosum; L.V, Left vagus; R.V, Right vagus; R.N, Recurrent nerve; L.C.C, Left cervical cardiac branch of vagus; R.C.C, Right cervical cardiac branch of vagus; R.A.B, Right aortic body; L.A.B, Left aortic body; R.P.B, Right pulmonary body; L.P.B, Left pulmonary body.

homologous structures adjacent to other vestiges of the branchial arch arteries has also been established.

The carotid bifurcation is not indeed the only situation in the human body in which tissue with similar structure and function to the carotid bodies is found. In the first place a small aggregation of such tissue has been described by Guild (1941) at the base of the skull, in relation to the jugular bulb, and has been termed the ' glomus jugulare '. Though its function has not been directly determined, its histological resemblance to the carotid body is close, and it is tempting to postulate an origin for it from the second arch artery, a portion of which persists in the adult as the stapedial. In the second place, as part of the paraganglionic theory, the existence of thoracic paraganglia in relation to the base of the heart and great vessels was recognized in the early part of this century, but little attention was paid to the

exact location of these structures, and they were interpreted merely as interesting examples of the capacity of the cells of the autonomic nervous system for migration and decentralization. More recent investigation, however, has established the constancy of occurrence of these cellular bodies in relation to the aortic arch, to the innominate artery, and to the pulmonary arteries (Nonidez, 1936, 1937); further investigation has confirmed the origin of these bodies in the fœtus from fourth and sixth branchial arch arteries (Boyd, 1937); whilst in the case of the aortic bodies their role in controlling respiration (Dripps and Comroe, 1944), and their proximity to pressor-receptor areas homologous with the carotid sinus, has been verified (Boyd, 1939), and their morphological homology with the carotid bodies completely established.

A brief account of the topographical anatomy of the aortic and pulmonary bodies is germane to this discussion (*Fig.* 152). The description which follows is largely based on the comparative studies of Nonidez (1936, 1937) and the embryological studies of Boyd (1937, 1939).

The aortico-pulmonary epithelioid bodies, best referred to as glomera, fall into two groups: aortic, situated above the arch of the aorta; and pulmonary, situated below the arch.

The aortic glomera are well localized and discrete paired organs. The right aortic glomus is situated in the angle below the subclavian artery at its origin from the innominate. It is innervated by the cervical cardiac branch of the right vagus, which also supplies the adjacent pressor-receptor area in the wall of the innominate artery, and it derives its blood-supply from that vessel. The left aortic glomus is situated on the anterior and upper aspect of the aortic arch close to the origin of the left subclavian, and is innervated by the cervical cardiac branch of the left vagus, which also innervates the adjacent pressor-receptor area in the wall of the aortic arch. This glomus derives its blood-supply from the adjacent aorta. These two glomera are derivatives of their respective branchial fourth arch arteries.

The pulmonary glomera by contrast are poorly localized. The specialized glomus tissue is somewhat dispersed around the base of the heart, and a paired arrangement is not readily discernible, for though there are two main aggregations of glomus tissue these lie centrally, and one above the other.

The superior glomus lies above and behind the bifurcation of the pulmonary artery, the inferior lies posteriorly in the sulcus between the ascending aorta and the pulmonary conus. The former derives its nerve-supply from the cervical cardiac and recurrent branches of the left vagus, and its blood-supply from the aorta; whilst the latter is innervated by the cervical cardiac branch of the right vagus, and derives its blood-supply from the left coronary artery.

Glomus tissue and related pressor-receptor areas are known to develop on the sixth arch arteries of the human fœtus, but with the alteration of circulation associated with the closure of the specialized ductus arteriosus it is probable that the pulmonary branchial pressor-receptor areas largely retrogress. The glomus tissue, too, loses its primary connexion with the sixth arch arteries, and in the rearrangements associated with pulmonary respiration loses, in addition to its original blood-supply, something of its definition and identity. None the less the branches of innervation from left and right vagi indicate with reasonable certainty that the superior pulmonary glomus derives from the left branchial sixth arch artery, and the inferior from the right.

It therefore appears fully established that tissue histologically, physiologically, morphologically, and embryologically identical with that of the carotid bodies occurs in the superior mediastinum in man, and it follows that the occasional occurrence of tumours arising from the aortico-pulmonary glomera is to be anticipated. It is also to be anticipated that these tumours will resemble carotid body tumours in their morbid histology and clinical characteristics.

CASE REPORT

HISTORY.—A. C., an insurance agent, first attended the Middlesex Hospital in 1942 when aged 22 years. He complained of a lump in the left side of his neck, causing pain radiating up the back of his ear. He was also troubled with diarrhœa. It appeared that in 1939 he had developed a rash and glands in his neck which had been diagnosed as German measles. The diarrhœa had developed in 1940, and he had since been under observation suspected of tuberculosis.

ON EXAMINATION.—There was enlargement of the left supraclavicular glands, and also of glands extending upwards into both anterior and posterior triangles on the left; all appeared fixed deeply, and the main mass in the supraclavicular region was adherent to the clavicle. Radiographs of the chest showed enlarged paratracheal glands, increased strial markings in the lung fields, and stippling of both apices. Sputum and fæces were normal. Hæmatological investigation showed a normal sedimentation rate and completely normal blood-picture. A barium meal showed no abnormality apart from a group of calcified glands in the right lumbar region and an accelerated evacuation time. Sigmoidoscopy initially showed little abnormality, but at a later date the appearances were those of a granular proctitis.

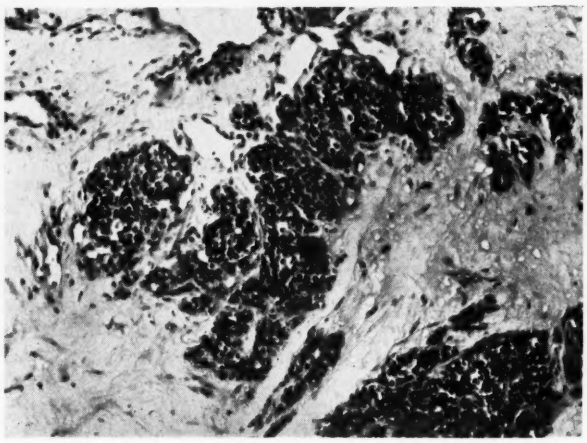

FIG. 153.—Section from glands of neck, showing clumps of cells intersected by numerous vascular clefts embedded in sheets of fibrous tissue undergoing hyaline degeneration. (× 105.)

A biopsy was taken from the cervical glands in the supraclavicular region. Histological examination of this showed subcapsular remnants of lymphoid tissue infiltrated by a network of branched, spindle-shaped,

and polygonal cells arranged in irregular sheets, cords, and clumps, and intersected by numerous vascular clefts and spaces, the whole mass of cells and sinuses being in turn intersected by relatively coarse fibrous trabeculæ (*Figs.* 153–155). The cellular elements of this infiltration had relatively abundant cytoplasm, acidophilic and slightly granular, and contained large, rather vesicular nuclei with well-defined chromatin network and one or more nucleoli. In the deeper parts of the gland the cellular elements were largely degenerate and were contained in clefts in a mass of fibrous tissue which was undergoing hyaline and calcific degeneration. The appearances were highly suggestive of an origin from a carotid body tumour, though no such tumour was demonstrable in the neck.

TREATMENT AND PROGRESS.—In that the condition was clearly inoperable it was decided to give deep X-ray therapy a trial. A tumour dose of over 4000 r was given to the supraclavicular region, though without apparent effect. A year later there had been some further increase in size and a further course of treatment was given, again without notable effect.

Since 1943 there has been little change in the condition of his cervical glands except for the appearance of radiographically recognizable calcification. A further biopsy in 1946 showed sheets of hyaline fibrous tissue

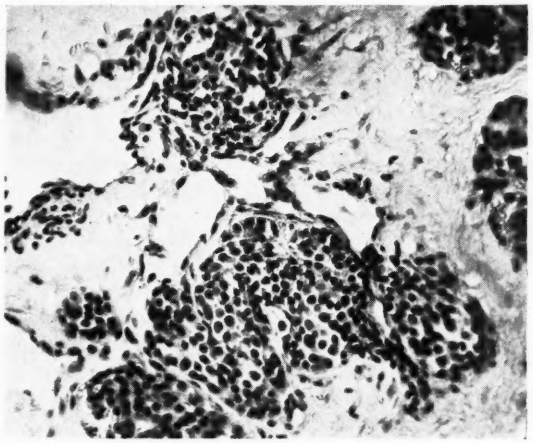

FIG. 154.—High-power view of the same section, showing the marked vascularity and intimacy of the vascular relationship typical of the alveolar type of carotid body tumour. (× 255.)

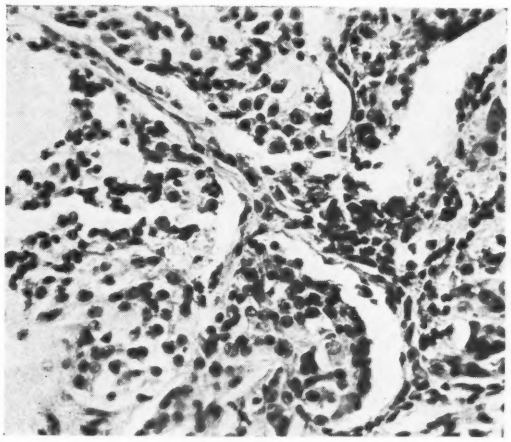

FIG. 155.—Section from the same tissue, showing polygonal and branched cells typical of a carotid body tumour and occasional mononuclear giant cells, a not uncommon feature in such tumours. (× 255.)

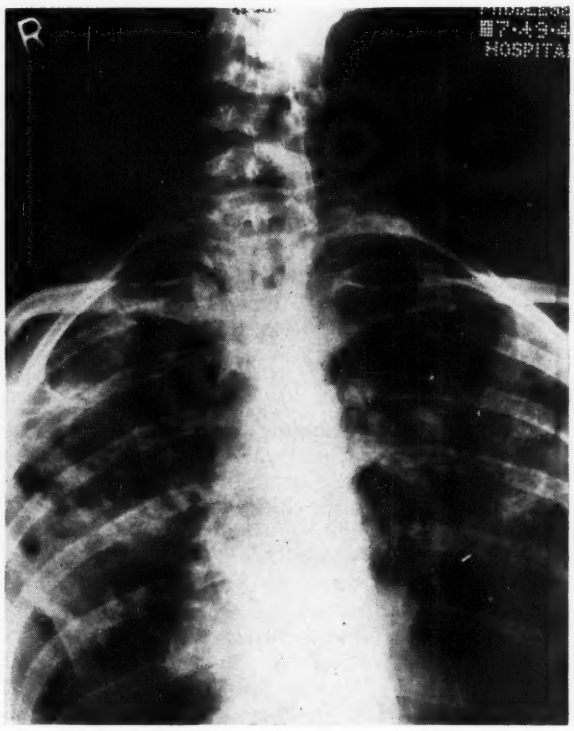

FIG. 156.—Radiograph of upper chest and neck, illustrating mottled shadows radiating from the lung hila, and calcified glands at the root of the neck.

FIG. 157.—Tomograph of the mediastinum, showing the mottled calcified shadow of the metastasis in the right lobe of the liver.

with extensive areas of calcification, but still areas of tumour cells similar to those appearing in the original biopsy. The patient's general condition has, however, steadily deteriorated. There has been a progressive increase in the mottling of the lungs associated with an increasing dyspnœa; a mild degree of dysphagia has developed associated with a slight stenosis of the œsophagus in the neighbourhood of the calcified glands at the root of the neck (*Fig.* 156); and a calcified mass 3 cm. in diameter has appeared in the right lobe of the liver (*Fig.* 157). The lung changes are essentially fibrotic and, in the absence of any evidence of tuberculous infection, the stimulus for this fibrosis must be presumed to be tumour cells similar to those responsible for the marked fibrotic reaction in the cervical glands. A similar fibrosis adjacent to these glands would appear responsible for the œsophageal stenosis, and it appears likely that the calcified mass in the liver is a metastasis possessing a similar histology.

DISCUSSION

Whilst it must be admitted that carotid body tumours exhibit considerable histological variation, and an appearance more easily recognized than described, nevertheless they possess a fundamentally constant structure. Carotid body tumours are cellular and vascular tumours. The cells are of moderate size, polygonal or tending to spindle shape, having finely granular faintly acidophilic cytoplasm, and a rather vesicular nucleus, with fairly prominent chromatin network and nucleolus. The cells tend to be aggregated in clumps and strands, intersected by numerous large capillary spaces.

Variation in morphology and distribution of the parenchymal cells in relation to the blood spaces allows distinction of alveolar, peritheliomatous, reticular, and cavernous types of tumour. Considerable variation is also shown in the degree of fibrosis. The majority of carotid body tumours are intersected by coarse fibrous trabeculæ, but not uncommonly this fibrosis may be extreme, large areas of the tumour being composed of fibrous tissue; this is very prone to hyaline degeneration and calcification.

Repeated biopsies from the tumour-mass at the root of the neck in the case here reported have consistently shown a parenchymal and vascular structure highly suggestive of origin from the carotid body. In the absence of a tumour at the carotid bifurcation this compels a diagnosis of tumour of one of the homologues of the carotid body. The lower cervical tumour-mass is clearly a metastatic involvement of lymph-glands, a conclusion borne out both by the histological appearances and by the discovery on clinical examination and subsequent radiography of a chain of similarly enlarged and subsequently calcified glands extending into the neck. The progressive infiltration from the hilum toward the periphery of the lungs, demonstrable in radiographs of the chest, can also be interpreted as due to a gradual infiltration by malignant cells, whilst the calcified mass in the liver would seem to be most reasonably interpreted as a blood-borne metastasis. It is to be concluded that the centre from which gradual centrifugal spread has occurred into the neck and lungs is in the mediastinum or lung root. A tumour so situated, and having such a histological appearance, could only arise from one of the aortico-pulmonary glomera.

It must be admitted as a point against the origin of this tumour from an aortico-pulmonary glomus that neither on plain radiography, nor on tomography, has any distinct tumour-mass been demonstrable in the superior mediastinum. However, this is a region notorious for the difficulties it presents in radiographic contrast, and it would be quite possible for a tumour 4 cm. in diameter in this situation to defy demonstration. It is therefore not impossible for the primary lesion in this case to be situated in the superior mediastinum; the direction of its centrifugal spread is strongly in favour of such an origin, and its histology strongly suggests derivation from an aortico-pulmonary glomus.

The clinical features of the growth also bear out its relationship to the better-known tumours of the carotid body. Carotid body tumours arise at any age, but are commonest in young adults, affecting the sexes equally. There is, however, a preponderance of males in those tumours which show more marked malignant characteristics (Monro, 1950). Carotid body tumours tend to be slow in growth, and their malignant features are debated, but there is no doubt that they are often at least locally invasive, becoming adherent to surrounding structures and liable to local recurrence after removal. There is really little doubt that glandular metastases may occur (Kopfstein, 1895; McComb, 1948), and it seems that authentic instances of distant metastases have also been recorded (Prendergrass and Kirsh, 1947; Donald and Crile, 1948). The case under consideration would appear to bear a close resemblance in its clinical features to a carotid body tumour. The tumour in this case affected a young male, was of slow growth, and exhibited a typical capacity for local infiltration. Metastases, too, were present, but the degree of malignancy implied by these is not without precedent amongst carotid body tumours.

Apart from the question of a carotid-body-like tumour, the principal lesions to be considered in the differential diagnosis of this case are carcinoma of the bronchus and thymic carcinoma. Bronchial carcinoma is usually of high malignancy, but gradation forms between it and adenoma of the bronchus are known to occur. In the latter a histological picture of masses and strands of polyhedral cells without true alveolar formation, but associated with marked vascularity and an 'endotheliomatous' appearance, and on occasion associated with marked fibrosis, has been described (Willis, 1948). A low-grade carcinoma from this source might, therefore, give a picture somewhat similar to that of the case in consideration. Thymic carcinomata, too, may on occasion exhibit 'endotheliomatous' appearances and not uncommonly desmoplastic properties (Ewing, 1942). Nevertheless, the histological appearance of the biopsy material is very strongly suggestive of an origin from the carotid body or similar tissue, and in that the clinical features of the case suggest a low-grade malignant lesion of the mediastinum, the diagnosis which most satisfactorily covers all features is that of tumour of one of the mediastinal homologues of the carotid body, namely, tumour of an aortic or pulmonary glomus.

As has already been pointed out, the occurrence of organs homologous with the carotid body leads

one to anticipate the occurrence of tumours resembling tumours of the latter, but situated other than in the carotid bifurcation. Such tumours have been described as arising from the glomus jugulare of Guild (1941) by Rosenwasser (1945) and Kipkie (1947), the latter instance being of particular interest in that it was associated with a simultaneous, normally situated, carotid body tumour. Two cases of aortic glomus tumour have also been described by Bloom (1943), but occurring in dogs. The precise origin in the mediastinum of the tumour here described has not been exactly determinable, for which reason it has been designated as an aortico-pulmonary glomus tumour. This is the first tumour of the aortic and pulmonary glomera to be recorded in man, but it is believed that the morphological, histological, and clinical evidence fully support the final diagnosis.

I wish to acknowledge the stimulating interest maintained by Sir Gordon Gordon-Taylor throughout the preparation of this paper; and the generosity of Mr. R. Vaughan Hudson for allowing me to publish this case, initially under his care. Dr. A. C. Thackray, of the Bland-Sutton Institute of Pathology, has proffered much helpful advice from the point of view of morbid histology; whilst to Professor J. D. Boyd, of the Department of Anatomy, London Hospital, I am in great part indebted for my concept of the morphology of the branchial glomera. My thanks are also due to Professor P. B. Ascroft, of the Surgical Unit, The Middlesex Hospital, for his keen interest in this work; and finally I wish to acknowledge the help of my colleagues on the Unit, Mr. L. P. LeQuesne and Mr. J. S. R. Golding, who have contributed much constructive criticism, and to thank Mrs. Trew for her excellent diagrammatic portrayal of the anatomy of the aortico-pulmonary glomera.

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SHORT NOTES OF RARE OR OBSCURE CASES

ENTEROLITHS IN A DUODENAL DIVERTICULUM

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THE majority of duodenal diverticula are of no clinical or pathological significance, and complications are rare. Ogilvie (1941) classified these complications as obstruction to the duodenum, common bile-duct, and pancreatic duct; diverticulitis, with the possible sequelæ of perforation, peridiverticulitis, duodenitis, and cholangitis; content of calculi, which may be enteroliths or gall-stones; and, finally, carcinomatous change. Frank (1944) reported a case of massive hæmorrhage from a duodenal diverticulum, and reviewed other cases of this further complication. The symptom-complex produced may be definite and severe, but it may be vague and ill defined, simulating a flatulent dyspepsia, cholecystitis, peptic ulcer, or colitis.

In the case now described the patient presented with obstructive jaundice and was found at post-mortem examination to have a duodenal diverticulum containing several hard enteroliths. There was also cholangitis and pancreatitis. These appeared at first to be due to the diverticulum, but the cut surface of the pancreas revealed a small carcinoma of the head of the pancreas.

CASE REPORT

HISTORY.—E. G. (R.I. No. 95439/48), aged 80, a retired agricultural labourer, was admitted to the Radcliffe Infirmary on Nov. 16, 1948. He had then been jaundiced for two weeks and had had several shivering attacks. There was a heavy feeling in his epigastrium, and he had recently lost weight. For some years he had suffered from mild prostatic symptoms of difficulty in starting micturition, dysuria, and nocturnal frequency. There was no relevant previous or family history.

ON EXAMINATION.—The patient was a wasted, feeble old man, deeply jaundiced. The enlarged gall-bladder was easily palpable in the distended abdomen, and was continuous with a smooth-edged liver 7 cm. below the costal margin. The urine was dark and contained bile: the stools were pale, and occult blood was present in moderate amounts. The prostate showed early benign enlargement. There were no other abnormalities on examination. The diagnosis made was of obstructive

jaundice, probably due to carcinoma of the head of the pancreas.

PROGRESS.—The patient was not fit for operation; his condition deteriorated, and he died eight days later.

AT AUTOPSY (R.I. P.M. 503/48).—The liver was enlarged and contained multiple small cholangitic abscesses. The distended gall-bladder, bile-ducts, and pancreatic duct were obstructed near the ampulla of Vater, but contained no stones. Bile could not be squeezed into the duodenum until a bristle had been passed into the ampulla and into the common bile-duct. There was a diverticulum, 6·5 × 3 × 2·5 cm., arising from the concave border of the duodenum 4 cm. distal to the ampulla, having a mouth 1·5 cm. in diameter. This diverticulum passed upwards, backwards, and to the left, displacing the pancreas and common bile-duct. It contained the larger enteroliths shown in the photograph (*Fig.* 158), several smaller ones, 0·2 to 0·3 cm. in diameter, and miscellaneous debris, including grape pips

FIG. 158.—The enteroliths.

and the remains of fruit skins. The head of the pancreas contained a small carcinoma approximately 1 × 0·5 × 0·5 cm. in size and adherent to the duodenum. There was a small chronic prepyloric ulcer 0·5 cm. in diameter. The lateral lobes of the prostate were enlarged and contained calculi. The remaining organs showed no significant changes.

HISTOLOGY.—The head of the pancreas contained a moderately differentiated adenocarcinoma, and there was a chronic fibrosing pancreatitis of the remainder of the organ.

Diverticulum: The wall consisted of mucous membrane, muscularis mucosæ, muscle coats, and serosa. There was no ulceration of the mucosa, but chronic inflammatory changes were present in the outer parts of the wall.

Liver: There was acute cholangio-hepatitis with bile retention and venous congestion.

The Enteroliths (*Fig.* 158): The larger stones were more than 6 cm. long, weighed 34 g., and were bile-stained and faceted. They were opaque to X rays. The specimen analysed had a small stalk or portion of a leaf vein at the centre, around which it had grown. It burnt away completely, leaving no inorganic residue, and was composed largely of bile acids with some fatty acids and traces of bilirubin and cholesterol and was therefore a cholic acid enterolith.

DISCUSSION

Edwards (1938) discussed three ways in which a duodenal diverticulum may produce jaundice—by direct pressure on the common bile-duct, by pressure of a secondary pancreatitis, and by cholangitis secondary to ascending infection in biliary obstructions. He remarked that any doubts as to direct pressure of the diverticulum causing jaundice are dispelled by the case described by Nicholson (1935). In the present case, however, the common bile-duct was obstructed by a carcinoma in the head of the pancreas, with secondary pancreatitis and ascending cholangitis.

The occasional association of a gastric ulcer and duodenal diverticulosis was noted by Bockus (1944).

Ogilvie (1941) described a concretion of relatively soft consistence in a duodenal diverticulum. It was brownish-yellow in colour, and was composed of alternating layers of yellow and brown material, together with a small amount of fibrous substance. Chemically it was composed of a mixture of cholesterol and fæcal matter. He reviewed three cases reported by Chomel (1710), Harley (1857), and Harris (1932), in which gall-stones were found in duodenal diverticula, but he was unable to find a previous report of a concretion in such a diverticulum.

Two examples of gall-stone in these diverticula have since been reported. The case described by Rankin (1942) simulated acute cholecystitis and cholelithiasis. A laminated stone over 5 cm. in diameter was seen on a confirmatory radiograph, and thought to lie in the gall-bladder: a cholecystogram was not carried out. At operation, however, the stone was found to occupy a diverticulum of the second part of the duodenum. Hare and Cattell (1944) described a case in which gall-stones in a diverticulum of the second part of the duodenum simulated gall-bladder colic. Glassmann (1929) gave an account, illustrated by radiographs, of the expulsion of a concretion from a duodenal diverticulum during routine roentgenological examination. This concretion was passed unknown to the patient and unfortunately not recovered, so that its composition will never be known.

A radiograph of the abdomen in the present case would presumably have revealed the opaque enteroliths, and a barium meal shown them to be in the region of the head of the pancreas. It is possible that the barium would have outlined the diverticulum in which they lay.

Hellström (1936) described the impaction in the jejunum of a cholic-acid enterolith, formed around a plum-stone in a duodenal diverticulum. He pointed out that these enteroliths are formed in the upper part of the small intestine, generally above a stricture, or in a diverticulum. He stated that all cases reported up to that time were in women.

Intestinal obstruction due to a fæcolith, which appeared to have developed in a duodenal diverticulum (Shaw, 1941), and in a duodenojejunal diverticulum (Goodall, 1948), has been reported.

The origin of stones in duodenal diverticula has been explained either by their formation around a gall-stone passed from the biliary tree, or as a result of stasis in the diverticulum. In the present case there was no evidence of biliary lithiasis, and although the opening of the diverticulum was 1·5 cm. in diameter, the central stalk or leaf vein in the analysed portion of the concretion and the miscellaneous debris found at autopsy seem to indicate that these concretions resulted from stasis. It is a matter for speculation whether the concretions expanded to fill the diverticulum, or whether this increased in size as the concretions grew.

SUMMARY

1. In the case now described a duodenal diverticulum contained several hard cholic-acid enteroliths.

2. There was also obstructive jaundice, cholangitis, and pancreatitis, but these were due to a small carcinoma in the head of the pancreas.

We wish to thank Mr. A. Elliot-Smith for permission to publish this case; Dr. A. H. T. Robb-Smith for his help and advice; Dr. G. A. C. Summers for the photograph; and Mr. J. R. P. O'Brien for the analysis of the concretion.

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ACUTE CHOLECYSTITIS, IN A CHILD AGED 4, TREATED BY CHOLECYSTECTOMY

REPORT OF A CASE, WITH A BRIEF REVIEW OF THE LITERATURE

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The British literature on cholecystitis in childhood is very scanty. Most of the published case reports and reviews of the subject appear in the American literature.

In this report, a case of acute cholecystitis is described in a boy aged 4 years. An acutely inflamed gall-bladder was found at an emergency operation to remove what was thought to be an acute appendix. The gall-bladder was removed and the child made an uninterrupted recovery.

THE LITERATURE

Mohr (1931), in an article on 'Acute Cholecystitis in Childhood', listed 150 cases which he had collected from the literature: most of the cases had occurred either during or after an attack of typhoid fever. He himself reported a case of acute cholecystitis in a 5½-year-old boy, who had suffered from paratyphoid fever three years previously. At operation, the gall-bladder was dull grey, distended, and acutely inflamed. No stones were found in the biliary system. After aspiration of 20 c.c. of purulent fluid from the gall-bladder, cholecystectomy was performed and the boy made an uneventful recovery. *B. paratyphosus* was cultured from the contents of the gall-bladder and the Widal reaction was found to be positive.

Mohr was of the opinion that cholecystitis in children could occur: (*a*) with cholelithiasis; (*b*) without stones, due to an infection of the gall-bladder via the portal stream with various organisms, such as the typhoid and paratyphoid bacilli, *B. coli*, cholera, etc., though most commonly the first two organisms.

Montgomery (1932) reported 3 personal cases of acute cholecystitis in children aged from 6 to 10 years. In one child, aged 7, suffering from repeated attacks of abdominal colic, an opacity which was noted in the straight radiograph of the abdomen was proved, after cholecystography, to be a stone in the gall-bladder. A barium enema and an intravenous pyelogram had already been carried out! Montgomery's impression was that all the infections of the digestive tract in children could give rise to acute cholecystitis. Gall-stones, too, must always be borne in mind, since they can be formed at all ages, and have even been found in a six-month-old fœtus.

Some people believe that trauma is important. Vollmer (1930) described a case following a blow to the abdomen with a football. Even the case described by Mohr (quoted above) seems to have been precipitated by a blow on the abdomen.

Potter (1928), in the most authoritative existing review of the subject, analysed all the cases in the

literature up to August, 1927. He found 226 cases, all of them in children under the age of 15. The first published case was that of Gibson in 1722. The commonest causes of acute cholecystitis in these cases were (*a*) typhoid fever, and (*b*) digestive tract disorders. He reported 4 personal cases. Two of these were due to gall-stones, and in 2 of the cases acute cholecystitis was correctly diagnosed before operation. All the cases were treated by cholecystectomy.

In a later article, Potter (1938) collected all the additional cases of acute cholecystitis in children which had been reported from August, 1927, to July, 1937. This gave a total of 432 cases, including a further 6 cases from his own practice.

In the British literature, Downie (1938) reported a case of acute cholecystitis in a 15-month-old infant as a complication of what appears to have been a simple gastro-enteritis. The provisional diagnosis was that of acute appendicitis, but at operation the gall-bladder was greatly distended and acutely inflamed. Some 30 c.c. of dark bile was aspirated from the gall-bladder and a catheter then inserted for drainage purposes. The infant made an uneventful recovery, showing very dramatic improvement after the relief of tension within the gall-bladder.

CASE REPORT

T. W., a male child aged 4, was admitted to hospital on July 24, 1949, with a history of diarrhœa and vomiting for some 36 hours previous to admission, accompanied by vague colicky abdominal pain localized around the umbilicus. The child had been "off colour" for the past four weeks, and during that time had suffered from recurrent attacks of colicky abdominal pain lasting anything from a few minutes to almost half an hour. On two or three occasions he had had loose motions, but nothing like the diarrhœa of the past 36 hours. Micturition was perfectly normal, but the mother stated that on the previous day the child's urine had been much darker in colour than usual. The bowels were acting normally and there was no history of any pale stools. The child had been off his food for the past four weeks, but his appetite was normally excellent. There was nothing significant in the child's past medical history apart from a tendency to recurrent attacks of tonsillitis.

The boy's sister, aged 9, had developed jaundice at the beginning of June this year (with dark urine and pale stools) after being "off colour" for some three weeks prior to this. The jaundice was transient, but, according to the mother, quite definite and had been confirmed by a medical practitioner.

On Admission.—A healthy-looking child, not visibly dehydrated. Temperature 99°; pulse 106; respirations 20. Slight icteric tinge was noticed in the sclera of both eyes. The tongue was clean and moist. The throat was clear and the tonsils were not enlarged. Chest examination revealed no abnormality. On abdominal examination the liver margin could be easily felt, but was well within normal limits for a child of his age. There was an area of tenderness over the right side of the abdomen just above McBurney's point and lateral to the umbilicus. Rectal examination was negative.

A provisional diagnosis of infective hepatitis was made. On the following day the child was perfectly well. The temperature had settled to normal and there was no abdominal tenderness at all. Two days after admission, the child had a recurrence of the abdominal colic early in the morning. This pain increased in severity and in the evening of the same day the child looked ill. The temperature had risen to 100·4° and the pulse to 140. The tongue was coated and on abdominal examination there was very marked local tenderness and rigidity in the right iliac fossa and a very definite palpable mass was present slightly above the true McBurney's point. Rectal examination was negative. In view of these findings, laparotomy was decided upon, the provisional diagnosis being that of acute appendicitis.

At Operation.—The appendix was found to be normal in every respect. The palpable mass which had been noted before the operation was found to be an acutely inflamed distended gall-bladder. No calculi could be felt anywhere in the biliary system. Cholecystectomy was then performed and the abdomen then closed in layers with a drain down to the gall-bladder fossa.

The post-operative course was completely uneventful. No penicillin or sulphonamide preparation was given and the child rapidly recovered.

Further investigations were made during the convalescent period. Culture of the fæces revealed only *B. coli*. The Widal reaction was negative in all dilutions for *B. typhosus* and *B. paratyphosus*. A complete blood-count showed: Hb 72 per cent; colour index 0·75; red blood-cells 4,980,000 per c.mm.; white blood-cells 12,000 per c.mm., with a normal differential count.

The Specimen.—The pathologist's report on the section of the gall-bladder was as follows: "The wall of the gall-bladder shows acute inflammation." Unfortunately the contents of the gall-bladder were never collected and sent for culture.

COMMENT

Most of the reported cases of acute cholecystitis in childhood presented as abdominal emergencies with colic, localized tenderness and rigidity, and often with a palpable lump in the right side of the abdomen. Almost all the cases have been opened up with the provisional diagnosis of acute appendicitis. The case reported above is no exception, though the slight jaundice which was noted by some of the observers should have put one on to the scent of gall-bladder disease.

Whether the jaundice was due to the attack of cholecystitis or to an attack of infective hepatitis, or whether the cholecystitis was a complication of infective hepatitis, remains a matter for speculation.

I wish to thank Dr. J. H. Follows, of the Royal Halifax Infirmary, for permission to publish this case; and Mr. I. Bruce, who undertook the operative treatment.

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A CASE OF TRIFID URETER AND SEGMENTAL HYDRO-URETER

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It has been stated that multiple ureters occur in 3 to 4 per cent of patients that come to pyelography or post-mortem (Colosimo, 1938). The large majority of these developmental anomalies take the form of a duplication of the ureter, and triplication of the ureter is a rare condition (Cambell, 1937). It is for this reason that the following case is being reported. Also it appears to be unique in that it presents an additional abnormality in the form of a large pouch at the lower end of the ureter, and an almost unrecognizable kidney at the upper end.

Smith (1946), in his excellent review of triplication of the ureter, classifies them into three main types: (1) Complete triple ureter; (2) Double ureter, with one bifid; and (3) All three ureters united and draining into the bladder through a single orifice—viz., 'trifid ureter'.

The case here described is a true trifid ureter of the third type in the above classification.

EMBRYOLOGY

The formation of a triple ureter may be explained by briefly surveying the earliest development of the ureter.

From the posteromedial wall of the mesonephric (Wolffian) duct, and near its junction with the cloaca, a bud appears at about the fourth week of embryonic life and grows dorsally (*Fig.* 159 A). As

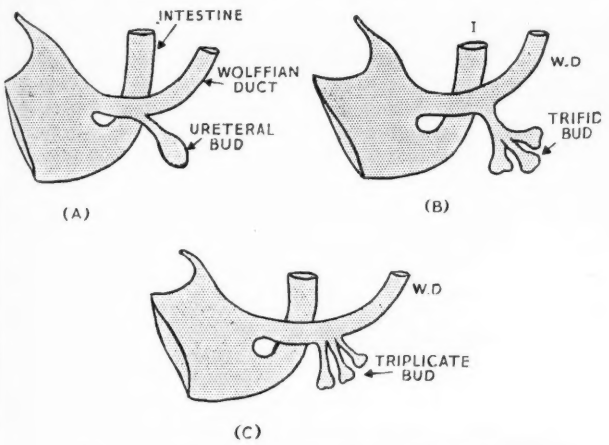

Fig. 159.—Diagrammatic attempt to show development of: (A) Normal ureter, (B) Trifid ureter, and (C) Triplicate ureter.

it enlarges it comes into contact with the metanephrogenic tissue, which is gradually displaced cranially. This cranial end of the bud divides into a cranial and caudal portion (major calices). These in turn give rise to further branches, which eventually come to form the collecting tubules.

If, however, the splitting of the blind end of the ureteral bud is abnormal, it is not difficult to visualize that multiple divisions may result in the formation of bifid or trifid ureters (*Fig.* 159 B). Again, depending on the site of the division in relation to the ureteric junction with the mesonephric duct, degrees of abnormality can occur varying from a bifid pelvis, to complete duplication or triplication of the ureter, and it seems reasonable to regard all these abnormalities as varying degrees of the same developmental fault (*Fig.* 159 C).

In the present case, no recognizable renal tissue was found, and the divisions of the ureter showed interesting cystic dilatations (*see Fig.* 163). The significance of these is difficult to assess, but may possibly mark the sites of unsuccessful attempts at further subdivision (i.e., into minor calices and collecting tubules).

CASE REPORT

History.—W. M., a male, aged 35, when first seen in January, 1947, gave a history of pain in the lower part of the abdomen (more marked on the right side),

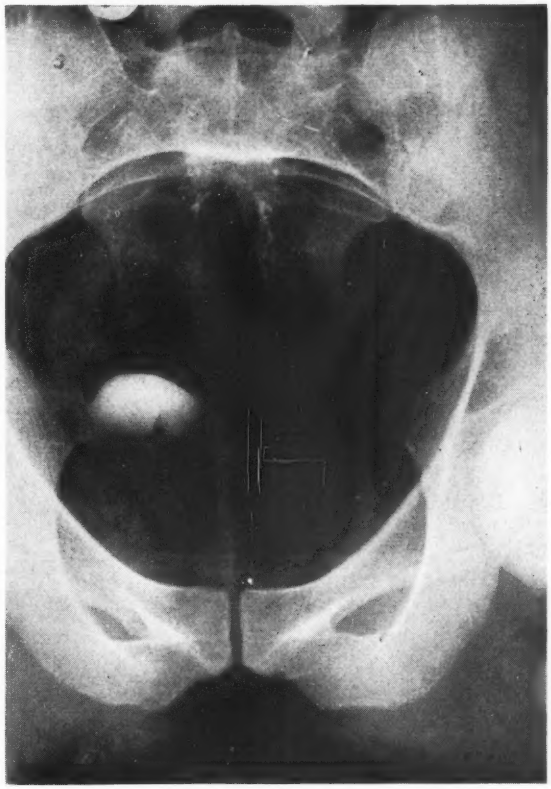

Fig. 160.—A plain radiograph showing an opacity on the level of the right ischial spine.

frequency of micturition, dysuria, and occasional attacks of hæmaturia, extending over the course of eleven years. Otherwise he had led an active life as a factory worker.

In 1945, for these symptoms, he had been seen by a surgeon, who told him that he had a stone in the bladder which was shown on an X-ray plate (presumably similar

FIG. 161.—A radiograph showing the ureteric catheter coiled in the segmental hydro-ureter.

FIG. 162.—A radiograph of the appearance after the injection of radio-opaque material.

FIG. 163.—Retrograde pyelogram showing the trifid ureter.

in appearance to *Fig.* 160), but without the confirmation of a cystoscopy. Following operation he was informed that no stone was present, but that " a blood-clot behind his bladder had become calcified ". An injury at football, when he was kicked in the perineum some years previously, was thought to account for this diagnosis. As the symptoms described above persisted he was referred by his doctor for further investigation.

ON EXAMINATION.—The patient was a well-built man of healthy appearance. The only abnormal physical signs were slight suprapubic tenderness more marked to the right of the midline, and rectal examination was painful high up to the right. A well-healed suprapubic scar was present.

A plain radiograph of the urinary tract showed there to be an opacity in the bony pelvis, about $1\frac{1}{4} \times \frac{3}{4}$ in. in size, at the level of the right ischial spine (*Fig.* 160). No secretion could be detected on the right side following intravenous pyelography, but the left kidney appeared normal.

Cystoscopy revealed a severely inflamed bladder wall. The left ureteric orifice was of normal appearance and the efflux looked clear. The right ureteric orifice, however, was slightly deformed and no efflux was observed. Through it a catheter could easily be passed, and was considered to have reached the kidney. But on radiography it was found that this catheter had, in fact, entered a circular pouch and coiled itself neatly around its walls (*Fig.* 161). Radio-opaque material was then injected up the catheter, and showed an interesting developmental abnormality. The ureter was grossly distended at its lower end to form a circular cavity about $1\frac{3}{4}$ in. in diameter, and into which the catheter had previously curled. At its upper extremity the ureter divided into three branches, each capped by a small dilatation (*Figs.* 162, 163).

At this time the urine contained pus and red blood-corpuscles, and on culture produced a heavy growth of

coliform bacilli. Careful search was made for tubercle bacilli on many occasions with negative results.

TREATMENT.—In view of the severity and persistence of the urinary infection, operation was undertaken on Feb. 15, 1947. Through a right loin incision the ureter was isolated with its three branches. Around their extremity a small piece of fibrous tissue appeared to be the only evidence of kidney formation. An approach to the lower end of the ureter was made through a right oblique muscle-splitting incision. The distended portion of the ureter was mobilized, and divided as it entered the bladder. The complete specimen was then removed (*Fig.* 164).

FIG. 164.—Drawing of the specimen removed at operation. The pouch at the lower end has been opened. No recognizable renal tissue was present.

PROGRESS.—Recovery from operation was uneventful, and his frequency and dysuria improved from the second post-operative day. Subsequently, he has had occasional but short-lived attacks of urinary infection, which are becoming both less severe and less frequent.

DISCUSSION

No sign or symptom is pathognomic of ureteral abnormality. As in this case, diagnosis is usually made following radiological investigation of a patient presenting with symptoms of pain, frequency of micturition, dysuria, or hæmaturia, or any combination of these. Schmutte (1929), Frank (1933), Schroter (1937), and Perrin (1927) have reported cases of trifid ureter, but only in Perrin's case was a correct pre-operative diagnosis made, the abnormality in the others being discovered at operation or autopsy.

This case is unique in the additional presence of a distension at the lower end of the deformed ureter. In a discussion of Grantham's paper in 1930, Moore suggested that "large localized dilatations of the lower ureter without an actual sac and orifice should not be considered as a diverticulum at all but might be more properly termed a 'localized megalo-ureter'".

More recently Culp (1947) and Pratt, Gahagan, and Fischman (1947) repeat this plea for more accurate terminology.

The ureteric dilatation of the present case should therefore be described as a segmental hydro-ureter. The origin of similar cases previously described (Willecke, 1890; Janke, 1925; Moore, 1930; Bugbee, 1931), has been attributed to dilatation immediately above a stricture at the ureteral orifice. This case, however, resembles Dodson's (1944), in which the large size of the sac must have been caused by regurgitation of urine through the ureteric orifice, since the kidney was aplastic. As in his case, the retention of alkaline urine, and deposition of phosphatic material, gave rise to a shadow on radiography of the bony pelvis (*Fig.* 160). This appearance no doubt led to the original diagnosis of vesical calculus, and emphasizes only too strongly the need for cystoscopic examination of shadows believed to lie within the bladder before undertaking cystotomy.

A further possible explanation of this condition may be found in the work of Campbell Begg (1946). He has demonstrated that the excretory activities of the ureter occur by means of a "cystoid" mechanism. Varying numbers of these cystoids (but constant for the individual), may be found in the course of the ureter as dilatations having a detrusor action on the propulsion of urine down the ureter. It does not seem unreasonable to suppose that a segmental hydro-ureter may be an irreversible representation of the cystoid commonly seen at the lower end of the ureter, although such a well-marked dilatation, circular rather than oval in appearance in the present case, is somewhat difficult to reconcile. Furthermore, there is no evidence that it ever did propel urine into the bladder in spite of its rather thick and muscular walls. It does, however, give food for thought.

SUMMARY

1. The incidence and classification of triplication of the ureter is reviewed.

2. An attempt is made to explain this deformity embryologically.

3. A case is described with a trifid right ureter and segmental hydro-ureter, in the absence of recognizable renal tissue.

4. The symptomatology and diagnosis are briefly discussed, together with a consideration of the cause of segmental hydro-ureter.

I wish to thank Mr. Vernon Pennell, under whose care this patient was admitted to hospital, for much helpful advice in the preparation of this paper.

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DOUBLE GALL-BLADDER

REPORT OF A CASE

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DOUBLE gall-bladder is an uncommon anomaly, and, although there are now quite a number of cases in the literature, ours is probably only the second recorded which has been diagnosed by cholecystography and subsequently confirmed at operation and by pathological examination.

CASE REPORT

H. A., aged 67 years.

PREVIOUS HISTORY.—In 1906 the patient had enteric fever while serving as a regular soldier in India.

HISTORY OF PRESENT ILLNESS.—Attacks of colicky epigastric pain started three weeks before admission.

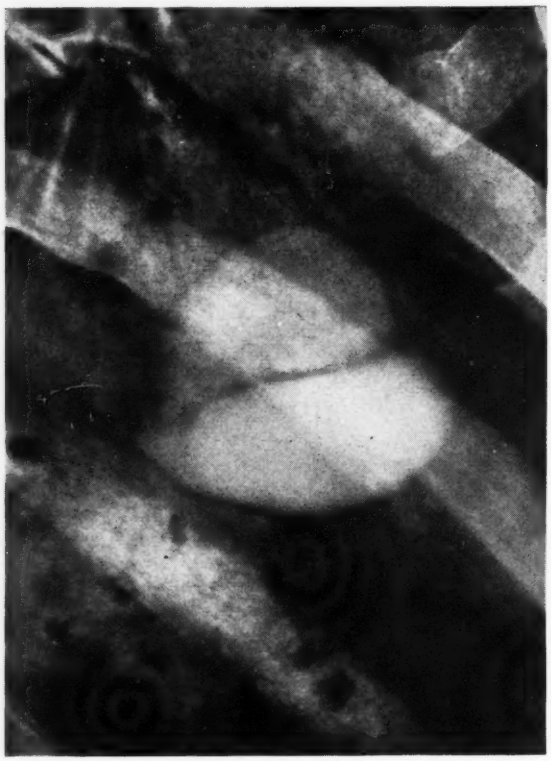

FIG. 165.—Cholecystogram, Nov. 5, 1948, taken by Dr. A. S. Johnstone. The gall-bladder was seen duplicated and concentrated fairly well.

There was no previous history of significant indigestion or flatulence. Shivering and 'cold sweats' accompanied the attacks of pain. Pain was relieved when he turned on to his left side. Since the onset of pain the patient had lost his appetite. During the two weeks previous to admission he had noticed that the whole of the right side of his abdomen was "sore and tender to touch". Vomiting had been frequent during the three days previous to admission. His bowels had been opened normally throughout the illness.

ON EXAMINATION (Oct. 26, 1948).—The patient was obese, garrulous, and restless: his face was flushed and his tongue dry and furred. Temperature 99°; pulse 108; respiration 24. The abdomen moved fairly well on respiration. There was tenderness and rigidity over the whole of the right side of the abdomen. No tumours were palpable on abdominal and rectal examination.

W.B.C. 7400 per c.mm.

It was considered that the patient was suffering either from acute cholecystitis or acute appendicitis. In view, therefore, of the history of pain for three weeks and the localization of the signs to the right side of the abdomen, it was decided to treat the patient by starvation and sedatives. He improved on this régime. A cholecystography was done by Dr. A. S. Johnstone on Nov. 5. A double gall-bladder which concentrated the dye was revealed (*Fig.* 165).

AT OPERATION (Nov. 10).—Kocher's incision. The gall-bladder was found to be reduplicated, with two cystic ducts, but these were so closely adherent it was not possible to tell whether they united before entering the common duct. The gall-bladders were closely adherent to each other and the inner one was embedded in the right lobe of the liver. No evidence of acute or chronic inflammation was found in the region of the gall-bladder or bile-ducts. The cystic ducts and cystic artery were ligatured and the gall-bladders removed.

The right iliac region was then examined and many œdematous adhesions were found here between the omentum, cæcum, and appendix. The appendix itself was swollen, red, and closely adherent. No pus was found. The appendix was removed. The retrocæcal region and right kidney pouch were drained by rubber dams, the rest of the abdominal wound was closed.

It seemed probable that the recent acute illness had been caused by an acute inflammatory appendicitis and not acute cholecystitis.

Progress after operation was uneventful.

MORBID ANATOMY.—The surgical specimen (*Fig.* 166) consisted of two small gall-bladders which, although quite separate entities, were loosely attached by fibrous and

adipose tissue (*Fig.* 167). They were of approximately the same size, each measuring 5 cm. in length by almost 5 cm. at the broadest diameter when fully opened. About 1 cm. of cystic duct was attached to each sac; the ducts were in close proximity and, although separate structures, were fairly firmly adherent near their origins. The mucosa of both sacs was green owing to bile staining and in one there was early lipoid flecking (*Fig.* 166).

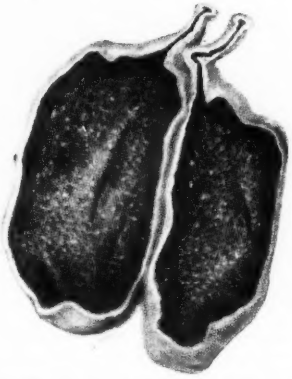

FIG. 166.—Gross surgical specimen showing double gall-bladder with separate cystic ducts. One sac (right) shows early cholesterosis.

FIG. 167.—Histological section through mid-portion of the two opened sacs to show their attachment by loose connective tissue. (× 3.)

HISTOLOGY.—Both gall-bladders have rather attenuated muscle coats and show some fibrosis, which, although patchily distributed through the whole thickness of the walls, is particularly prominent in the mucosæ. The epithelium is well-preserved, shows bile imbibition, and dips downwards into the muscle, and even into the serosa, in several places; one gall-bladder shows early cholesterosis (*Fig.* 168). Moderate diffuse and focal infiltration by lymphocytes, with some plasma cells and eosinophils, is present in the walls of both sacs. The serosal vessels are telangiectatic and numerous, and some are thick-walled. The appearances are those of mild chronic cholecystitis in both gall-bladders, with early cholesterosis in one.

DISCUSSION

Guyton (1946), in a review of the literature, found only 40 recorded cases of double gall-bladder proven by autopsy or operation, and added a case of his own. Meyer, Dowlin, and Reinglass (1949) recorded a further case, which, with ours, makes a total of 43. In addition, a number of cases visualized by cholecystography, but not operated upon, have been recorded.

Boyden (1926) classifies the anomaly into two groups: vesica divisa or cleft gall-bladder, with two sacs emptying into a common cystic duct; and vesica duplex, composed of two gall-bladders each with its own cystic duct. The two cystic ducts either unite to form a common cystic duct or empty separately into the common bile-duct. Our case and that of Meyer and others are examples of vesica duplex; in neither was it certain what happened to the cystic ducts beyond the operation site. Guyton found in only 29 of the 40 case reports sufficient detail to enable him to classify them; 24 were examples of vesica duplex, and in 16 the cystic ducts joined the common bile-duct separately.

Only a few cases of double gall-bladder which have been diagnosed radiologically have been recorded. Scott, Sanes, and Smith (1941) consider their case to be the first recorded where a double gall-bladder was visualized radiographically and subsequently proved at operation and by pathological examination; our case would therefore appear to be the second.

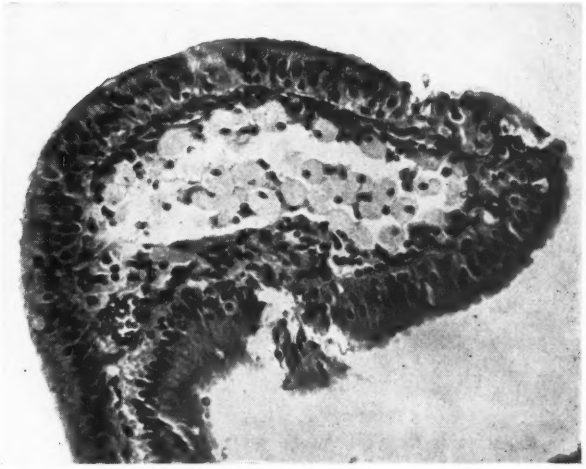

FIG. 168.—Histological section of the mucosa of the sac showing cholesterosis. (× 110.)

SUMMARY

A case of double gall-bladder of vesica duplex type is described. The diagnosis was made by cholecystography and was confirmed at operation and by pathological examination.

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FULMINATING GANGRENE OF THE PENIS

REPORT OF A CASE

By A. G. McPHERSON

FULMINATING gangrene of the penis is a clinical entity, closely allied to fulminating gangrene of the scrotum. It is distinct from penile gangrene complicating general or local disease, e.g., urinary extravasation, venereal ulceration, gross trauma, etc. Classically the onset is sudden and dramatic in a previously healthy individual. The condition has also been referred to in the literature as 'spontaneous gangrene', 'idiopathic gangrene', 'streptococcal gangrene', etc., but is perhaps best known in this country as 'Fournier's gangrene', after his classic description of the condition.

FIG. 169.—Condition on Sept. 22, 1949, three days after onset.

The following case, recently observed, is recorded in view of the rarity of the condition.

CASE REPORT

G. S., a male farmworker, aged 67, was admitted to the Royal Infirmary, Sheffield, on Sept. 21, 1949, complaining of pain and swelling of the penis and scrotum, which had started two days previously. He gave a negative history of past disease, apart from bilateral inguinal hernia of thirty years' duration, for which he wore a truss. Three days before the onset of symptoms he had noticed a small scratch on his penis, which may have been caused by his truss, which was old and worn.

ON EXAMINATION.—He looked a very ill man. His tongue was heavily coated, his breath fœtid, and his mental faculties blurred. Temperature was 101° F.; pulse 108.

The scrotum and base of the penis were markedly reddened and œdematous, a faint erythema extending to the thighs and abdomen. The skin of the shaft of the penis was gangrenous and showed a yellowish-brown discoloration, with some areas of superficial ulceration from which exuded a serosanguinous fluid. A line of demarcation was already visible. *Fig.* 169 shows the condition on the day following admission.

Culture of the exudate gave, under aerobic and anaerobic conditions, a pure growth of penicillin-sensitive *Streptococcus pyogenes* Group A.

Blood-count showed a microcytic anæmia (Hb, 65 per cent; C.I., 0·9) and a slight polymorph leucocytosis (leucocytes 12,000 c.mm.).

Blood non-protein nitrogen was 83 mg. per cent. The urine showed a cloud of albumin; sugar nil.

Blood-Wassermann was negative.

PROGRESS AND TREATMENT.—In view of the severity of the toxæmia, treatment with penicillin (120,000 units 6-hourly) and sulphamezathine (1 g. 6-hourly) was initiated without awaiting the results of the bacterial cultures made on admission. Within 24 hours there was a marked improvement in the patient's general condition, which no longer gave cause for anxiety. This improvement was steadily maintained and the pulse and temperature had returned to normal within a few days. The local condition, however, did not show so dramatic a change. The œdema of the penis and scrotum increased in the next few days, and the erythema became more extensive and much more intense, beginning to fade only after four days' treatment. There was, however, no extension of the gangrene, the line of demarcation becoming sharply defined at the original site, as the dead tissue changed colour, becoming black, leathery, and dry. *Fig.* 170 (Sept. 24) shows the increase of erythema and the colour change in the dead skin.

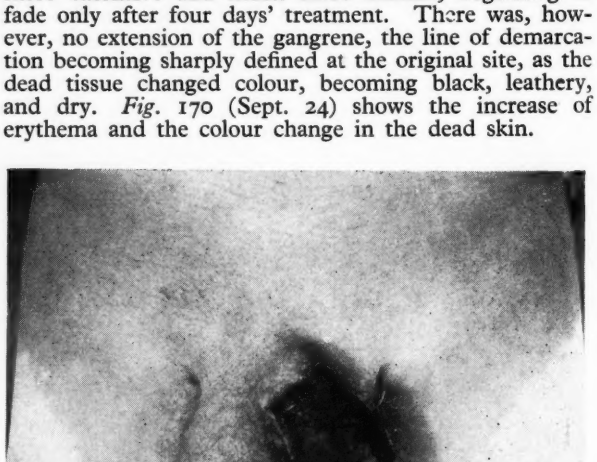

FIG. 170.—Condition on Sept. 24, five days after onset. Shows spread of erythema.

Separation of the sloughs was slow and was encouraged by baths and eusol dressings, once the acute stage had passed. By Oct. 17 all the dead tissue had separated, leaving a raw granulating area over most of the body of the penis. At this stage a persistent œdema remained and reparative surgery was further postponed until this should have diminished.

On Oct. 28, although œdema was still marked in the distal redundant prepuce, which had survived, the raw area was covered, after excision of exuberant granulations, partly by turning back the redundant prepuce as a cuff, and the remainder by three rotation flaps, two from the scrotum and one from the suprapubic region. Healing was satisfactory. *Fig.* 171 shows the post-operative result. It is to be noted that the œdema of the preputial cuff is still present; this has steadily diminished. The power of erection has returned.

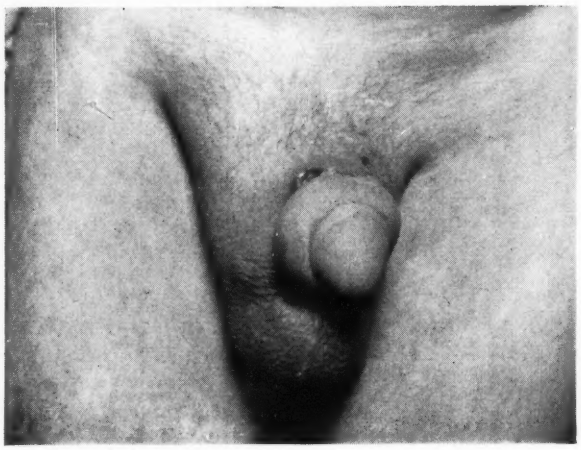

FIG. 171.—Condition on Nov. 15. Healing is complete. Marked œdema of prepuce remains.

DISCUSSION

This case is an example of fulminating streptococcal gangrene, the organisms having gained an entrance through a scratch in the skin, the result of an incident of minor trauma a few days earlier. The sudden onset in a previously healthy man, the extremely rapid development of gangrene, and the absence of the usual predisposing causes of gangrene, are the three characteristics emphasized by Fournier (1883, 1884), who postulated an infective cause.

A trivial scratch or abrasion is often the inciting cause, though cases have been reported following surgical procedures, e.g., circumcision. The hæmolytic streptococcus is the organism that has been implicated in the majority of cases reported, either alone or in combination with a staphylococcus. *B. coli*, diphtheroids, *B. fusiformis* and *Sp. Vincenti*, and *Cl. Welchii* are among the many other organisms which have been held to blame in other cases, and it would seem probable that a variety of organisms may, on occasion, produce the condition.

The mortality-rate in the past has been high, McCrea (1945) finds a 17 per cent mortality in 123 cases of fulminating gangrene of the penis, collected from the literature. His table shows that the mortality has dropped in recent years, and it is certain that with the new antibiotics now available the prognosis is vastly better. The response in the case reported here, to penicillin and sulphamezathine, was dramatic, toxæmia was rapidly relieved, and no spread of the gangrene occurred. It was of interest that the area and the intensity of the erythema increased, although the infection was clearly under control, due presumably to the continued diffusion of erythema-producing toxin already formed.

The survival of the distal prepuce was noteworthy and simplified the plastic repair.

I wish to express my thanks to Professor R. St. Leger Brockman for his permission to publish this case.

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LEIOMYOSARCOMA OF THE JEJUNUM PRESENTING AS PERITONITIS

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LEIOMYOSARCOMA of the small intestine is rare; Brink and Laing (1933) estimated that only 6 to 8 per cent of small-bowel sarcomata are myogenous, and Lewis (1939) could only find 30 cases described in detail in the literature. Cases presenting as peritonitis have been described, but this is an unusual complication.

CASE REPORT

HISTORY.—A man, aged 59, was admitted on June 30, 1949, complaining of severe abdominal pain mainly in the hypogastrium and left iliac fossa. The pain had started suddenly 4½ hours previously and had been continuous since onset. For two months he had had intermittent subumbilical pain, unrelated to meals and never severe; he had lost 5 lb. in weight in 3 to 4 months and complained of loss of energy, and tiredness. His appetite had been good, with no nausea or vomiting, his bowels had been regular, and his motions normal in colour.

ON EXAMINATION.—He was pale and shocked. Temperature 99·8° F., pulse 112, respirations 20. Heart and lungs, no abnormality. Tongue, moist. Abdomen, resistant all over and tender, particularly on the left side below the umbilicus. Liver dullness was not diminished. Nothing abnormal was found on rectal examination.

A diagnosis of peritonitis, probably due to a ruptured diverticulum of the colon, was made.

AT OPERATION.—Under thiopentone, gas, oxygen, and lateral intercostal block, the abdomen was opened by a subumbilical midline incision. Free fluid was found on opening the peritoneum. A mass was felt in the right iliac fossa; it was at first thought to be an appendix abscess. On closer examination it proved to be a soft friable tumour 3 in. in diameter, arising from

the antimesenteric border of the jejunum about 4 ft. from the duodenojejunal junction.

The transverse colon was adherent to the tumour, but separated easily from it, revealing a ragged perforation in the tumour, from which some mucoid material

FIG. 172.—Photograph of the specimen removed at operation; the site of the perforation is not clearly seen, but it is near the lighter area on the photograph in the middle of the tumour. This area is a piece of fat from the great omentum which shows evidence of fat necrosis as a result of the perforation.

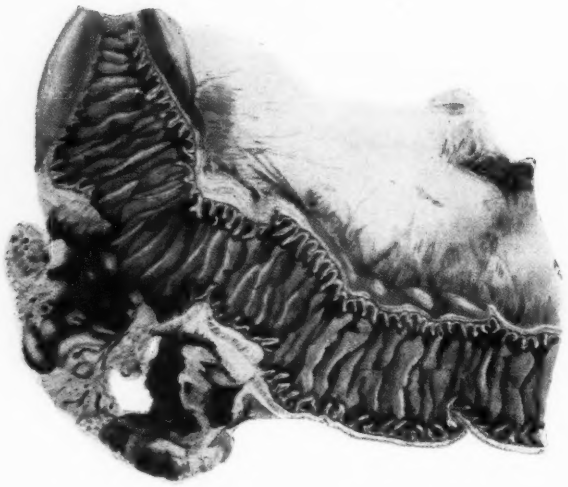

FIG. 173.—Painting of the specimen. The appearance that the growth is in two parts has been produced by the way in which the bowel has been cut. The white thickening of the wall of the gut is seen to merge into the main tumour mass.

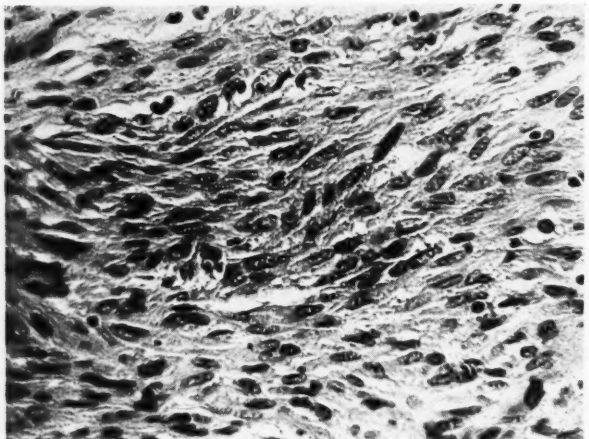

FIG. 174.—A section from one edge of the tumour, showing the appearances of a leiomyoma. (× 262·5.)

FIG. 175.—A section from the sarcomatous part of the growth, showing tumour giant cells, mitoses, and hyperchromatism. (× 262·5.)

escaped. Firm enlarged glands were felt in the mesentery and two very small nodules of doubtful significance were felt on the superior surface of each lobe of the liver.

A 12-in. loop of jejunum, including the tumour and a wedge of mesentery with the enlarged glands, was resected. The tumour was attached to the peritoneum of the overlying abdominal wall, and this part of the peritoneum was excised with the growth; the cæcum, which was also adherent to the tumour, separated easily from it. End-to-end anastomosis of the divided jejunum was done and the wound closed around a corrugated rubber drain.

Two pints of blood were given slowly during and after operation.

The post-operative course was uneventful; the drain was removed on the third day. The patient was discharged from hospital on Aug. 6. A blood-count was not done on admission, but on July 8 it was: Hæmoglobin 88 per cent; Leucocytes 17,500, 84 per cent being neutrophils. The patient was seen again o Sept. 23. He was very well and had gained 21 lb. i weight. His blood-picture was: Hæmoglobin 97 pe cent; Leucocytes 14,200, neutrophils 67 per cen lymphocytes 28 per cent, monocytes 4 per cent, eosinophils 1 per cent.

PATHOLOGY OF SPECIMEN.—

Macroscopical Appearance (*Figs.* 172, 173).—Twelve inches of jejunum. Two inches from one end there is a firm white thickening of a portion of the wall with a perforation at this site ½ in. in diameter leading through a mass of tissue on the antimesenteric border of the bowel 3 × 2 × 1½ in. This mass is greyish-white, with some yellow and some hæmorrhagic areas. Enlarged glands are present in the mesentery up to ½ in. in diameter. The lumen of the bowel is not appreciably narrowed at the site of the tumour.

Microscopical Appearance (Dr. A. C. Thackray) (*Figs.* 174, 175).—Sections show replacement of the wall of the intestine by a tumour consisting for the most part of anaplastic sarcomatous growth, but with small areas composed of uniform well-differentiated smooth muscle-fibres. The undifferentiated areas show hyperchromatism,

marked variation in size of the nuclei, and moderate numbers of mitotic figures; there are areas of hæmorrhage and necrosis present. The lymphatic glands in the mesentery are not invaded.

Diagnosis: Leiomyosarcoma of the small intestine.

DISCUSSION

Andersen and Doob (1933), reviewing 19 cases of leiomyosarcoma of the small bowel, found that the commonest symptoms are vague abdominal pains, the passage of tarry stools, and anæmia, and other reports confirm these findings. A movable abdominal tumour has been palpable in about half the cases reported. Perforation of the growth is uncommon—Frank, Miller, and Bell (1942) report a case of spindle-cell sarcoma presenting as an intestinal perforation, and Pugliatti (1934) described a perforation of a leiomyosarcoma.

The X-ray findings are rarely helpful in making a diagnosis unless ulceration of the mucosa and cavitation has occurred, when it may be possible to demonstrate the cavity.

Pathology.—Leiomyosarcomata occur more frequently in the jejunum than in the ileum, arising from the smooth muscle of the bowel wall. Usually they grow away from the lumen, producing a tumour on the outer surface of the bowel, sometimes growing into the mesentery, without narrowing the lumen, and intestinal obstruction is rare. Central degeneration and hæmorrhage into the growth tends to occur; if associated with ulceration through the mucosa at the site tumour blood finds its way into the bowel and gives rise to melæna (Golden and Stout, 1941). Necrosis of the growth with perforation and peritonitis happens infrequently. Metastases are present in about 30 per cent of cases generally in the liver.

CONCLUSION

This case of a leiomyosarcoma of the jejunum is recorded as a reminder that new growths of the small intestine may give rise to 'unexplained melæna'. The clinical features and radiological findings are often not helpful in making a diagnosis, which may only be revealed on laparotomy.

I wish to express my thanks to Mr. C. J. B. Murray for permission to publish this case; to Miss Margaret Harvey Moore for the painting of the specimen; and to Dr. A. C. Thackray for the microphotographs.

FOOTNOTE.—It is now known that the patient died on March 7, 1950, with multiple intraperitoneal metastases.

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ACCIDENTAL SECTION AND SUCCESSFUL RESUTURE OF A BRONCHUS

BY J. R. BELCHER, LONDON

A CASE recently reported by Lloyd Griffiths (1949), in which an end-to-end anastomosis of a bronchus was performed after the excision of a fractured cartilage, prompts the reporting of another case of successful anastomosis performed in rather different circumstances.

CASE REPORT

HISTORY.—The patient, a man aged 20, reported complaining that for one year he had had pain in the left side of the chest associated with a chronic cough productive of 1 to 2 oz. of purulent sputum daily. He had no dyspnœa, nor had he had hæmoptyses. The significant features in his past history were that he had had measles and whooping-cough at the age of 4 years, and a left mastoidectomy had been performed when he was 17.

ON EXAMINATION.—His general condition was good. There was no clubbing or cyanosis, and apart from scattered moist sounds over his left lower lobe, there were no abnormal physical signs; he was expectorating 2 to 3 oz. of purulent sputum daily.

Bronchograms showed no abnormality on the right side, but gross saccular bronchiectasis of all the segments of the left lower lobe, with minimal dilatation of the lingular bronchi (which has since become more apparent) (*Fig.* 176). His vital capacity was 3400 c.c. Bronchoscopy showed no abnormality, apart from rigidity of the left lower-lobe bronchi. It was decided to perform a left lower lobectomy.

AT OPERATION (Jan. 31, 1949).—Dissection lobectomy was performed without incident, the left lower-lobe

FIG. 176.—Pre-operative bronchogram showing gross lower-lobe bronchiectasis. This radiograph has been reversed.

bronchus having been clamped early. After division of the pulmonary vessels the clamp was readjusted before division of the bronchus, in an effort to leave as little stump as possible, but it was inadvertently moved up on to the main bronchus above the upper-lobe orifice, and the bronchus was divided at this point. Alternatives of pneumonectomy or anastomosis after resuture of the lower lobe stump then presented: as the bronchial vessels were still thought likely to be intact, the latter course was taken. The lower-lobe bronchus was re-clamped and sewn with interrupted thread, and the lower lobe removed. An end-to-end anastomosis of the divided main bronchus just above the level of the upper-lobe orifice was then performed, also with interrupted thread, all the posterior row of sutures having been inserted before any of them were tied. At the completion of the suturing there was still a small inaccessible leak in the posterior wall, but when an intercostal muscle-graft had been sewn round the junction, this leak ceased. The chest was drained for forty-eight hours post-operatively, but there was no significant leak of air. The upper lobe collapsed after forty-eight hours, but re-expanded immediately after bronchoscopy. (The site of anastomosis was inspected and the lumen was not grossly narrowed.)

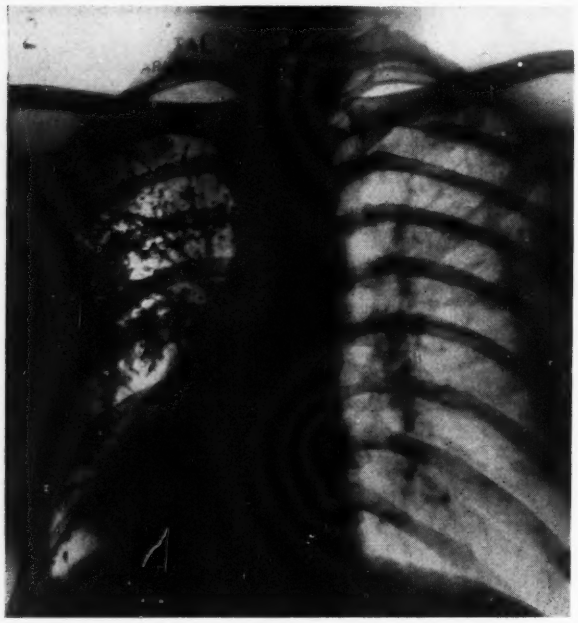

FIG. 177.—Post-operative bronchogram, showing stump of lower-lobe bronchus, above which is the site of anastomosis. This radiograph has been reversed.

After this the patient made a good recovery and was discharged on Feb. 24.

Further bronchograms were made on May 5 (*Fig.* 177), at which stage the patient was well, vital capacity 2400 c.c., and had a trace of sputum only. Auscultation revealed a just detectable expiratory rhonchus over his left upper lobe. The site of anastomosis was just visible on the bronchogram, but no gross stenosis was present, an it seems fair to assume that this is now unlikely to develop.

He last reported on June 30, saying that his symptoms were unaltered since his previous visit and that he was back at work.

My thanks are due to T. Holmes Sellors, under whose care this patient was admitted, for permission to publish this case.

REFERENCE

GRIFFITHS, J. LLOYD (1949), *Thorax*, **4**, 105.

GASTRIC RESECTION IN SITUS INVERSUS TOTALIS

BY RICHARD E. SHAW

WEST MIDDLESEX HOSPITAL

SURGICAL operations in the presence of situs inversus have recently been the subject of a study by Blegen (1949). He found that 158 of such operations had been recorded, 5 of which were performed on the stomach. These five operations were :—

1. Gastro-enterostomy for gastric ulcer (Kelly, 1920).
2. Gastro-enterostomy for prepyloric carcinoma (Allen and Allen, 1936). This patient died three weeks after the operation.
3. Closure of a perforated duodenal ulcer (King, 1941).
4. Partial gastrectomy for gastric ulcer (Kapustin, 1945).
5. Partial gastrectomy for prepyloric carcinoma (quoted by Blegen, who saw the patient in consultation).

The case reported below appears to be the third recorded instance of a gastric resection performed in the presence of situs inversus.

CASE REPORT

HISTORY.—A 65-year-old gardener was seen at the West Middlesex Hospital by Dr. N. F. Coghill in July, 1948, complaining of intermittent pain below the left costal margin of twelve months' duration, which had been worse during the preceding fortnight. There was loss of appetite, but no nausea or vomiting. At times the abdomen felt distended. He had lost 2 st. in weight during the same period, and felt he had no energy. There was some shortness of breath on exertion, and he complained of frequency of micturition and difficulty in passing his water. His previous health had been good.

ON EXAMINATION.—The patient was a well-built, elderly man who had clearly lost some weight. His complexion was sallow. The apex beat was felt on the right side inside the midclavicular line. The heart-sounds were normal, and a blowing systolic bruit was heard at the apex. His blood-pressure was 135/75 mm. Nothing abnormal was found in the respiratory system with the exception of crepitations at both bases. Abdominal examination revealed that the liver dullness was on the left side. There was a little tenderness in the epigastrium, but no mass was felt. On rectal examination the prostate was found to be moderately enlarged.

The following investigations were carried out :—

Barium meal and follow-through: "The stomach is on the right side of the abdomen. The gastric emptying time is normal. There is a large filling defect of the pars media of the stomach, no doubt due to carcinoma. Passage through the small intestine is normal. The intestines are transposed, the cæcum and appendix being

on the left side. Passage through the large intestine is normal."

Radiography of the chest: "Dextrocardia; there are mild chronic bronchitic changes in both lungs. At the apices there is some abnormal shadowing, more marked on the left side than the right, which is probably due to tuberculous infiltration. Its activity is doubtful."

Blood-count: Hæmoglobin 12·2 g. (83 per cent). Red blood-cells 4,350,000 per c.mm. Mean corpuscular hæmoglobin 28 γγ.

Electrocardiography: The findings were typical of congenital dextrocardia.

AT OPERATION.—On Aug. 16 the abdomen was explored through a midline epigastric incision. There was complete transposition of the viscera, the stomach and spleen lying on the right side, and the gall-bladder, the larger lobe of the liver and the cæcum and appendix on the left. On the anterior wall of the body of the stomach was a large carcinoma, some 2½ in. in diameter. There was no evidence of glandular, hepatic, or peritoneal metastases. The duodenum was moderately dilated, so that its calibre approximated to that of the pyloric part of the stomach. A subtotal gastrectomy of the posterior Polya-Hofmeister type was performed, and the abdomen closed.

Apart from some degree of post-operative bronchitis a good recovery was made from the operation, and he was discharged home on Sept. 2. The tumour was reported on histological examination to be a columnar-cell carcinoma with a papilliform structure.

In July, 1949, eleven months after his operation, the patient was in good health and there was no evidence of recurrence of the neoplasm.

COMMENT

It is not easy to explain why the patient complained of pain below the left costal margin. The localization of pain in situs inversus is a puzzling subject since the pain is frequently felt on the side of the body opposite to that of the diseased organ. For instance, in acute appendicitis, the pain may be felt in the right iliac fossa, so that the difficulties of diagnosis are further increased. This paradox has been explained on the following lines. Although the viscera are transposed to the opposite side, it is believed that the component parts of the nervous system are not reversed, so that if referred pain is experienced it will be felt on that side which the viscus occupies in a normal person. Returning to the case reported above, it may be that some similar mechanism accounts for the left-sided pain, although the growth occupied a position on the right side of the body. The subject of visceral pain perception is ill understood, and it would be unwise to speculate further.

The operation itself presented little difficulty. Many of the manipulations which are normally performed semi-automatically required a little extra thought, and it was found advantageous to perform most of the operation standing on the left side of the patient.

I wish to express my thanks to Mr. John Scholefield for his assistance in composing this paper.

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PERFORATED JEJUNAL ULCER

BY JAMES S. JEFFREY, EDINBURGH

THE perforation of a jejunal ulcer into the general peritoneal cavity is a rare and rather lethal condition. Jejunal ulcer itself (*syn.* gastrojejunal ulcer, stomal ulcer, secondary peptic ulcer) follows a gastro-enterostomy in 10 per cent of cases, and when Wright (1935) made a study of the subject on behalf of the Association of Surgeons he noted that of 458 secondary ulcers proved at operation 48 were met with as acute perforations into the general peritoneal cavity. The customary treatment for acute jejunal perforation is simple closure, followed usually by a more radical operation at a later date. Simple closure carries a high mortality: 23 per cent in Wright's series, and 17·6 per cent in the series of Toland and Thompson (1936). As the method of treatment in a poor surgical risk, simple closure may be the only treatment feasible, but a more radical procedure may be justifiable in favourable circumstances, as it was in the following case:—

CASE REPORT

HISTORY.—R. F., aged 57, male, was admitted to the charge of Professor Walter Mercer in the Edinburgh Royal Infirmary as an emergency on April 26, 1949. He had been seized with sharp epigastric pain six hours previously, and collapsed at his work as a clerk. On admission he was shocked and obviously in severe pain. The abdomen was very tender in the epigastrium and left hypochondrium, muscles were board-like, liver dullness was diminished, and there was a complaint of pain in the left shoulder.

There was a clear history of previous duodenal ulceration, with perforation and simple closure in 1945. He had remained symptom-free for the following six months and then began to show evidence of recrudescence of the ulcer and of pyloric stenosis, and in 1946 a posterior gastro-enterostomy was performed. At this operation the first part of the duodenum was noted to be deformed and an ulcer crater was palpable, the stomach was large and congested, and there was marked pyloric stenosis. An isoperistaltic posterior gastrojejunostomy was performed, using catgut and without clamps. Immediately prior to this operation a fractional test-meal had shown almost complete absence of free acid, and a slowly rising curve of total acidity reaching 80 (0·292) in 2½ hours after an initial 10 (0·036); so that gastro-enterostomy seemed a very suitable operation for a 54-year-old man with pyloric stenosis and a relatively low acidity. And so it proved for three years, for he kept well until 1949 and gained 3 st. in weight.

Three weeks before the present episode he again had some dyspeptic symptoms. There had been one bout of hæmatemesis, and a tendency to constipation. When seen six hours after the sudden onset of severe abdominal pain it was not difficult to suspect perforation

of a gastrojejunal ulcer. It was thought that gastrectomy might be indicated, and resuscitation and staff measures were taken with that in view.

AT OPERATION (J. S. J.).—Under pentothal, cyclopropane, and oxygen anæsthesia (Dr. F. Holmes) the abdomen was opened through a fresh midline supraumbilical incision. There was a small amount of non-purulent free fluid in the abdomen. The stomach was moderately enlarged, with gross pyloric stenosis, and the duodenum scarred but not œdematous. The posterior gastro-enterostomy was inspected and a free perforation of a jejunal ulcer was at once apparent. There was a small clear-cut circular hole, 0·5 cm. in diameter, in the middle of an œdematous area on the anterior wall of the efferent loop of jejunum, about 3 cm. beyond the stoma. The stoma was mobilized from the transverse mesocolon, and occlusion clamps placed across the afferent and efferent limbs of jejunum and across the stomach side of the stoma. The jejunum was divided across the two limbs and an end-to-end anastomosis of the jejunum performed with interrupted catgut stitches. Thereafter a partial gastrectomy was carried out. The duodenum was divided and invaginated just distal to the stenosed pylorus. The proximal third of the stomach was anastomosed to the jejunum about 3 in. distal to the end-to-end anastomosis of jejunum, in an isoperistaltic retrocolic Hofmeister-Polya method. The rent in the transverse mesocolon was sutured to the stomach side of the anastomosis. There was not a great deal of free fluid, and the abdomen was closed in layers without drainage.

PROGRESS.—The patient made a very satisfactory recovery and seemed no more affected by the operation (which took 90 minutes) than other men of his age after partial gastrectomy for peptic ulcer. He had one pint of blood, intravenous glucose-saline, and gastric suction for 48 hours. Three months later he was symptom-free again and back at work.

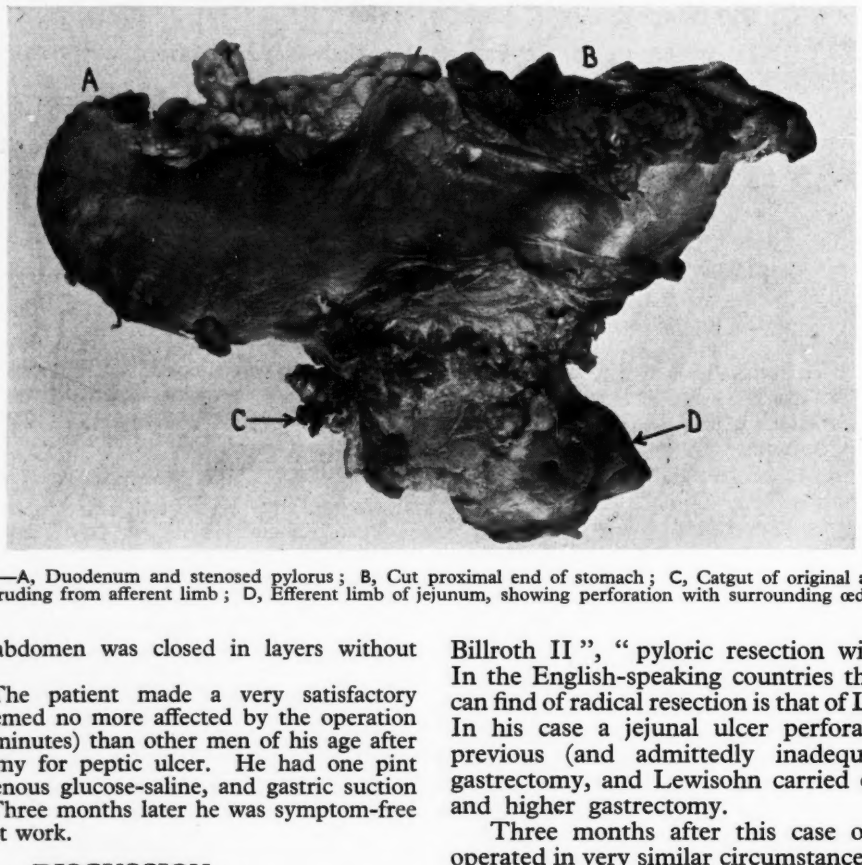

FIG. 178.—A, Duodenum and stenosed pylorus; B, Cut proximal end of stomach; C, Catgut of original anastomosis protruding from afferent limb; D, Efferent limb of jejunum, showing perforation with surrounding œdema.

DISCUSSION

The resected specimen (*Fig.* 178) shows a perforation at the commonest site, i.e., not at the stoma itself but on the efferent limb of jejunum. An interesting feature was the presence at the stoma of a length of the original catgut used in the anastomosis, still firmly attached at one end. This catgut was very coarse and swollen, and possibly a relic of unsatisfactory war-time catgut. It is doubtful, however, if this unabsorbed catgut played any part in the jejunal ulceration, because the stoma itself was not ulcerated. It is more likely that the ulcer was due to the effect of gastric acid on the efferent limb of the jejunum, even though the gastric acidity at the time of the original gastrojejunostomy was known to be relatively low.

Toland and Thompson in 1936 reviewed the 103 cases then reported of free perforation of gastrojejunal ulcers. On the question of treatment they noted that simple suture carried a mortality of 17·6 per cent, and usually required secondary operation. By virtue of its simplicity it is applicable to the largest number of cases. Suture combined with disconnexion of the gastrojejunostomy is a reasonable procedure provided the pylorus is patent. Toland and Thompson state that their most remarkable feature with respect to treatment of acute perforation of gastrojejunal ulcer was the fact that in 17 cases wherein "pyloric resection" was carried out there was only 1 death. The case reports of these resections mostly come from the German literature of the 1930's, and are noted as "pyloric resection with Billroth II", "pyloric resection with Polya", etc. In the English-speaking countries the only record I can find of radical resection is that of Lewisohn (1934). In his case a jejunal ulcer perforated following a previous (and admittedly inadequate) Hofmeister gastrectomy, and Lewisohn carried out jejunectomy and higher gastrectomy.

Three months after this case of mine I again operated in very similar circumstances. This second patient (aged 49) was seized with acute abdominal pain and a perforated stomal ulcer was suspected: he had had a gastro-enterostomy performed sixteen years previously and latterly had been having severe indigestion. I found, however, that the perforation in this instance was duodenal—apparently the original

duodenal ulcer had never healed. He did have a posterior gastrojejunostomy in situ (it had been done by the late Sir David Wilkie), but the stomal opening had shrunk to the size of two lead pencils. I undid the stoma, closed the small aperture in the jejunum, and carried out a partial gastrectomy (retrocolic Hofmeister-Polya), after dividing the duodenum distal to the duodenal perforation. This patient, too, made an excellent recovery.

British surgeons have never shown enthusiasm for the operation of partial gastrectomy for perforated duodenal ulcer, because we believe that simple closure is sufficient to cure a certain number of cases, and because 'circumstances' are seldom quite right: it is the middle of the night; the patient is not in good shape; the registrar doing the operation does not care to embark on such a procedure for fear of criticism if the outcome is unsatisfactory. For perforated jejunal ulcer, jejunectomy and gastrectomy is probably the operation of choice provided the patient is relatively young and in good condition, and provided three other factors are present—a surgeon with experience in the technique of gastrectomies, a competent anæsthetist, and readily available supplies of blood and other resuscitative measures.

SUMMARY

A case is described of acute perforation of a jejunal ulcer following previous operation for peptic ulceration. In such cases, and if circumstances are favourable, the method of treatment most likely to secure immediate and ultimate cure is resection of the segment of jejunum and partial gastrectomy.

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REVIEWS AND NOTICES OF BOOKS

British Medical Association Proceedings of the Annual Meeting, 1949. Pp. 468 + xxvi. 1950. London: Butterworth & Co. (Publishers) Ltd. 25s.

THE profession as a whole will continue to be grateful to the editor of the *British Medical Journal* for producing such a fine volume containing the proceedings of the Annual Meeting of the Association which was held at Harrogate in July, 1949.

The set-up and presentation of the various papers and discussions is excellent and the index is concise, practical, and correct. All these factors make the volume a most useful one, especially for reference.

We sincerely hope that the B.M.A. will continue the practice of publishing a volume such as this every year.

Penicillin. Its Practical Application. Under the General Editorship of Professor Sir ALEXANDER FLEMING, M.B., B.S., F.R.C.P., F.R.C.S., F.R.S., Professor Emeritus of Bacteriology, University of London; Principal, Wright-Fleming Institute of Microbiology, St. Mary's Hospital Medical School, London. Second edition. 5½ × 8½ in. Pp. 491 + xiv, with 63 illustrations. 1949. London: Butterworth & Co. (Publishers) Ltd. 30s.

A GREAT deal of water has passed under the penicillin bridge since the now well-known first edition of this book appeared three years ago, and it would appear from many chapters of this new second edition that much of the water has changed to procaine.

Evidence of careful revision is obvious in nearly every chapter of the book and the overall result is not only a more comprehensive survey of the subject but also at the same time a more selective one.

The intervening period has seen the acquisition of a great deal of knowledge regarding both penicillin itself as a substance and its myriad clinical applications. This knowledge is well described particularly in the 'general' chapters and has obviously led in the 'clinical' chapters to a far greater unanimity of opinion in respect both of indications for use and methods of administration.

As Sir Alexander Fleming himself points out in his preface, such lack of complete agreement on these points as still exists simply shows that there are still some problems waiting to be solved. Additions to the book—amounting in all to some 100 pages—give ample evidence that solutions to others have duly been found. Two excellent, if brief, chapters on Penicillin Sensitivity and Penicillin Resistance are a valuable appendix to the book. A new chapter on the use of Penicillin in Acute Infectious Diseases has also been added and modern trends are met by appendices on Streptomycin, Aureomycin, and Chloromycetin—all of which help to round off a book that certainly more adequately than any other of its kind provides a mine of information for bacteriologist and clinician alike. This edition is undoubtedly a considerable advance on its predecessor.

Medullary Nailing of Küntscher. By LORENZ BÖHLER, M.D., Director of the Hospital for Accidents in Vienna; Professor of Surgery at the University of Vienna. First English edition, revised by the author. Translated from the Eleventh German edition by HANS TRETTER, M.D., Trenton, N.J. 6¾ × 10 in. Pp. 386 + xi, with 1261 illustrations. 1949. London: Baillière, Tindall & Cox. 38s. 6d.

FOR many years Böhler was conservative in his treatment of fractures. This is one of the two chief reasons why his teaching was held in such great respect in Great Britain: the other was his attention to detail, which found eloquent expression in his famous book. The gradual revival of open operation for certain types of injury left him relatively unmoved, though he was forced to concede the merits of the Smith-Petersen pin. His enthusiastic reception of Küntscher's medullary nailing of fractures is therefore remarkable and very nearly intemperate. In 1944 he added a third volume to his standard work on fractures, devoted exclusively to the Küntscher method, and an English translation of it is now available. It runs to almost 400 pages and contains over 1200 illustrations.

Böhler was quick to realize the dangers as well as the advantages of intramedullary nailing, and that success depends on the careful choice of cases, the proper timing of operation in relation to the general and local condition, and on scrupulous precision in operative technique.

His method of presentation is familiar. No detail is omitted; even the methods of preparation of the developing and fixing solutions for rapid radiography are there.

Headings and important caveats appear in bold type. The result is a book that repels the casual reader but is indispensable for the surgeon who takes a serious interest in the treatment of fractures and is meditating on the types of injury in which intramedullary nailing would appear to be advantageous. This is not the occasion for discussion of the place of Küntscher's method in the surgery of fractures; that is a question to be hammered out by the men who do the work. Böhler is one of them, and he has performed a valuable service in drawing attention, if with prolixity, to the need for quite exceptional care in the employment of a technique which, whatever its virtues, must always entail hazards not found in more conservative practice.

Neoplasms of Bone and Related Conditions. Their Etiology, Pathogenesis, Diagnosis, and Treatment. By BRADLEY L. COLEY, M.D., Attending Surgeon, Bone Tumor Department, Memorial Hospital for Cancer and Allied Diseases; Assistant Professor of Clinical Surgery, Cornell. 7 × 10 in. Pp. 765 + xiv, with 389 illustrations. 1950. New York: Paul B. Hoeber Inc. (London: Cassell & Co. Ltd.) £6 10s.

THIS large, heavy volume devoted to the study of bone tumours is written by a surgeon who has devoted a large part of his surgical life to this important subject. The mantle of the father has fallen on the son. It is very appropriate that the son should have dedicated this book to his father, the late Dr. William Bradley Coley.

The aetiology, pathogenesis, diagnosis, and treatment of bone tumours are discussed in a most comprehensive manner and many clinical cases are described and illustrated.

The author has had a unique experience in America, for he has worked in a Bone Tumour Department and has made the best of his opportunities.

It is interesting to note that Coley's mixed toxin is not advocated in the treatment of bone sarcoma; it appears to have gone out of fashion in America, as it has done elsewhere.

Although the bibliography is extensive and comprehensive, it is made up almost exclusively of American references; we do not see the names of Fairbanks or Willis in the index of personal names, which seems a little odd.

The whole format and design of the volume is good and the type clear. We hope the next edition will appear in two volumes.

Acute Appendicitis and Its Complications. By FREDERICK FITZHERBERT BOYCE, M.D., Assistant Professor of Clinical Surgery, Tulane University of Louisiana School of Medicine. 6 × 9 in. Pp. 487 + xxii, with 78 illustrations. 1949. New York: Oxford University Press (London: Geoffrey Cumberlege) 70s.

ALTHOUGH many books have been written on appendicitis, yet few have been devoted solely to the problem of acute appendicitis and its complications. Dr. Boyce writes with matured clinical experience as his background; to have investigated 6441 cases of acute appendicitis is no mean achievement, and this forms the very material of the book.

Dr. Boyce gives an excellent description of the many and varied bizarre types of acute appendicitis, and his lucid style is a great help to the reader. It might be thought that with the extended use of antibiotics acute appendicitis is no longer a problem, yet this is far from the truth for, as the author explains, in the United States over 5000 persons die each year from acute appendicitis.

The clinician, especially the surgeon, has much to learn from this important monograph, which is full of solid clinical facts which are not too well known. The illustrations are well chosen and well produced, the references are comprehensive and accurate and comprise all the important articles which have been published in America and England.

A first-class book of reference on the subject of acute appendicitis.

The 1949 Year Book of General Surgery (August 1948–July 1949). Edited by EVARTS A. GRAHAM, A.B., M.D., Professor of Surgery, Washington University School of Medicine; etc. 4⅝ × 7 in. Pp. 707, with 216 illustrations. 1949. Chicago: Year Book Publishers Inc. (London: H. K. Lewis & Co. Ltd.). 37s. 6d.

THIS useful book of general surgery contains, as always, a balanced account of the various new procedures which have been advocated by surgeons from different parts of the globe. Professor Evarts Graham has by careful selection brought before the reader those advances in the various branches of surgery which he considers merit attention.

For the busy surgeon this book is a real treasure, for he can peruse it and glean practical information in a few minutes, instead of spending hours reading through the original articles.

The editor is to be congratulated once again on producing a very interesting and useful volume.

The 1949 Year Book of Orthopedics and Traumatic Surgery. 4⅝ × 7 in. Pp. 464, with 238 illustrations. Edited by EDWARD L. COMPERE, M.D., F.A.C.S., Associate Professor of Surgery, Northwestern University Medical School. 1950. Chicago: Year Book Publishers Inc. $5.00.

THE present volume of this hardy annual contains much of interest to the orthopædic and traumatic surgeon. Now that the war years are receding, less and less is being published on military surgery, but there is still a vast amount of traumatic surgery, which seems to increase as the years roll on.

The problems which arise from cases of poliomyelitis are ever present with us, and this Year Book gives an up-to-date review of the availiable literature.

The volume offers a valuable and an important background to all the progress which has taken place in the field of orthopædic and traumatic surgery during the year 1949.

The 1949 Year Book of Neurology, Psychiatry, and Neurosurgery. Edited by ROLAND P. MACKAY, M.D., Professor of Neurology, University of Illinois; NOLAN D. C. LEWIS, M.D., Director, New York State Psychiatric Institute and Hospital; and PERCIVAL BAILEY, M.D., Professor of Neurology and Neurological Surgery, University of Illinois. 4⅝ × 7 in. Pp. 668, with 113 illustrations. 1950. Chicago: Year Book Publishers Inc. $5.00.

IT might be thought that the three sections of Neurology, Psychiatry, and Neurosurgery comprise too vast a field for one single volume, yet this is perfectly justified as each section overlaps the other. The neurologist and the psychiatrist are interested in their cases which are treated surgically. The neurosurgeon, too, is interested in many neurological and psychiatric problems which excite curiosity from the clinical standpoint.

The editors of the Year Book are to be congratulated on the manner in which they have selected for special consideration the important papers which have appeared in the year under review. Every phase of the three subjects has been carefully covered and the volume should prove of real value to all who are interested in neurological, psychiatric, and neurosurgical problems.

World medical literature to-day has developed enormous proportions and no specialist can hope to keep abreast of every book or article that gains publication. It is these Year Books which play an important part in bringing to the fore articles of special interest which may have escaped the notice of various experts in different lands.

Modern Trends in Orthopædics. Edited by Sir HARRY PLATT, M.D., M.S., F.R.C.S., Professor of Orthopædic Surgery, University of Manchester; etc. $6\frac{5}{8} \times 9\frac{5}{8}$ in. Pp. 497 + viii, with 222 illustrations. 1950. London: Butterworth & Co. (Publishers) Ltd. 45s.

THIS volume is a notable contribution to British orthopædic surgery. Harry Platt is at his best in discussing the evolution and scope of modern orthopædics; and he has gathered around him an able band of surgeons who have specialized in some branch of orthopædic surgery. John Charnley gives us the up-to-date methods of the treatment of fractures, including the use of the intramedullary or marrow nail of Küntscher for fractures of the upper third of the femur.

G. R. Girdlestone draws on his great clinical experience in presenting an excellent chapter on tuberculosis of bones and joints.

V. H. Ellis deals with pyogenic affections of joints and bones, and stresses the value of penicillin in cases of acute osteomyelitis.

Arthur Rocyn Jones, writing on congenital dislocation of the hip, considers that reduction by manipulation is more commonly undertaken than by operation. The Shelf operation is reserved for those cases only where there has been an early relapse of a reduction, delayed subluxation, or a large and shallow acetabulum.

Other chapters in the volume are devoted to such conditions as congenital deformities of the spine and limbs, chronic arthritis, tumours of bone and muscle, scoliosis, anterior poliomyelitis, and the bone dystrophies.

The chapters are well illustrated both with clinical photographs and radiographs. There is a useful and comprehensive index. We have come to look on the 'Modern Trends' series as most useful and interesting volumes and this one devoted to orthopædics is no exception.

Studies on Tumour Formation. By the late G. W. de P. NICHOLSON, M.A., M.B., B.Ch., late Professor of Pathology, Guy's Hospital, London. $6\frac{5}{8} \times 9\frac{5}{8}$ in. Pp. 637 + xii with 183 illustrations. 1950. London: Butterworth & Co. (Publishers) Ltd. 63s.

THIS book on tumour studies will interest surgeons, particularly those who are interested in surgical pathology, and there are many.

Nicholson published his tumour studies in *Guy's Hospital Reports* between 1922 and 1938, and everyone will agree that these studies are classics. They have now been printed in book form, so that they will be available to a larger medical public.

Nicholson was a clinical microscopist; in the diagnosis of tissues he was unsurpassed, and his opinion was sought after both at home and abroad.

This book, which makes fascinating reading, covers a wide range of subjects, including tissue malformations, pigmented nævi, accessory suprarenals, the hyperplasias, fatty changes of epithelium, primary carcinoma of vagina, heterotopic tumours, tumours with a twofold stroma, the teratomata, somatic development and tumour formation, and ovarian goitre.

This is an astonishing range of topics and yet each chapter is written in a clear and masterly way in which the author brings out his own knowledge of the subject.

Books on tumours are often dull to the mere surgeon, yet this book, like Bland-Sutton's *Tumours Innocent and Malignant*, is written in an interesting manner—so much so that one is often pleased to re-read the book. A fascinating volume.

Diagnosis and Treatment of Brain Tumour. By ERNEST SACHS, M.D., Professor of Clinical Neurological Surgery, Washington. Second edition. Pp. 552, with 348 illustrations. 1949. London: Henry Kimpton. £5 5s.

THE second edition of Professor Sachs' book is considerably increased in size; this is because he has incorporated his other book on the *Care of the Neuro-surgical Patient*. This is a wise move, as the care of the neurosurgical patient is an inseparable part of the diagnosis and treatment of brain tumours.

The book is written in that easy, lucid, matured style that is so characteristic of Professor Sachs. The new edition contains important sections on electro-encephalography and angiography, and the usefulness of these procedures is stressed but not over emphasized.

The clinical cases reported are numerous and the various illustrations are excellent and could not be bettered.

Neurosurgeons will always be indebted to Professor Sachs for this book, for they will turn to it when they require accurate knowledge regarding brain tumours and their treatment.

Fractures. By PAUL B. MAGNUSON, M.D., F.A.C.S., Professor of Bone and Joint Surgery and Chairman of the Department, Northwestern University Medical School, Chicago; etc.; and JAMES K. STACK, A.B., M.D., F.A.C.S., Assistant Professor of Bone and Joint Surgery, Northwestern University Medical School, Chicago; etc. Fifth edition. 6×9 in. Pp. 537 + xx, with 325 illustrations. 1949. Philadelphia and London: J. B. Lippincott Co. 55s.

THE fifth edition of this book, the first of which was reviewed in this JOURNAL in April, 1934, contains much new material, some of it derived from experiences in the recent war. There are a number of new chapters. One is concerned with what the authors call the "farmyard" treatment of fractures, by which they mean the treatment of injuries under primitive conditions when a surgeon may have to use ordinary articles of household equipment—a sort of glorified first-aid. This exposition, useful as it is, would have been more valuable had it formed part of a chapter on the basic principles underlying the treatment of fractures, whether primary or definitive, for it is knowledge of these principles rather than of the equipment used that is of chief importance. There are chapters by Dr. Loyal Davis on spinal cord injuries and on fractures of the skull which present an excellent outline of the important points in the recognition and treatment of these complex injuries. Their inclusion suggests that it might have been wise to add also a short account of a third rather special group of injuries—fractures of the face and jaw.

The descriptions of the mechanics of injury and of the rationale and methods of treatment are clear and precise and illustrated by excellent radiographs and diagrams. The authors' views are expressed with some dogmatism but it is permissible in a book of this size and in one that is intended not so much for the specialist as for the general practitioner and the young surgeon; had there been a full discussion of even the chief alternatives in treatment the work would have become unwieldy. There are noticeable divergences from the views commonly held by surgeons in Great Britain, such, for example, as the tendency in fractures of the upper limb to stress

the importance of accurate reduction of a fracture rather than the need for securing a good functional result without undue regard for anatomical perfection. Dr. J. S. Coulter has contributed two chapters on simple methods of physical treatment which will be found particularly valuable to the beginner.

This book has lost none of its virtures, and has been improved by re-editing.

BOOK NOTICES

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest to readers.]

The Surgical Treatment of Facial Injuries. By VARAZTAD HOVHANNES KAZANJIAN, M.D., D.M.D., Professor Emeritus of Plastic Surgery, Harvard University; etc.; and JOHN MARQUIS CONVERSE, M.D., Assistant Professor of Clinical Surgery (Plastic Surgery), New York University College of Medicine; etc. $6\frac{7}{8} \times 10$ in. Pp. 574 + xiv, with 746 illustrations. 1950. Baltimore: The Williams & Wilkins Co. (London: Baillière, Tindall & Cox.) 76s. 6d.

Principles and Practice of Plastic Surgery. By ARTHUR JOSEPH BARSKY, M.D., D.D.S., Attending Plastic Surgeon, Beth Israel Hospital, New York City; etc. $6\frac{7}{8} \times 10$ in. Pp. 499 + xii, with 1029 illustrations. 1950. Baltimore: The Williams & Wilkins Co. (London: Baillière, Tindall & Cox.) 76s. 6d.

A Short Textbook of Radiotherapy. By J. WALTER, M.A., B.M., M.R.C.P., D.M.R.E., Consultant Radiotherapist and Deputy Medical Director, Sheffield National Centre for Radiotherapy; and H. MILLER, M.A., Ph.D., F.Inst.P., Physicist, Sheffield National Centre for Radiotherapy. With a Foreword by J. L. A. GROUT. $5\frac{1}{2} \times 8\frac{1}{2}$ in. Pp. 444 + xii, with 199 illustrations. 1950. London: J. & A. Churchill Ltd. 28s.

Urological Surgery. By AUSTIN INGRAM DODSON, M.D., F.A.C.S., Professor of Urology, Medical College of Virginia, Richmond; etc. With contributions by 12 others. Second edition. $6\frac{3}{4} \times 9\frac{3}{4}$ in. Pp. 855, with 645 illustrations. 1950. London: Henry Kimpton. £4 15s.

Thrombosis. In Arteriosclerosis of the Lower Extremities. By EDWARD A. EDWARDS, M.D., F.A.C.S., Clinical Associate in Anatomy, Harvard Medical School; etc. Being No. 41 in *American Lecture Series*. $5\frac{1}{2} \times 8\frac{1}{2}$ in. Pp. 74 + x, with 33 illustrations. 1950. Springfield, Ill.: Charles C. Thomas. (Oxford: Blackwell Scientific Publications Ltd.) 15s.

The Hinge Graft or Ginglymus Implant. By ARNOLD K. HENRY, M.B. (Dubl.), M.Ch.(Hon.) Cairo, F.R.C.S.I., Emeritus Professor of Clinical Surgery in the University of Egypt; Professor of Anatomy in the Royal College of Surgeons, Ireland. $6\frac{5}{8} \times 9\frac{5}{8}$ in. Pp. 64 + viii, with 47 illustrations. 1950. Edinburgh: E. & S. Livingstone Ltd. 15s.

Die Liquordiagnostik in Klinik und Praxis. By Prof. Dr. HANS DEMME, Hamburg. Second edition. $6 \times 8\frac{7}{8}$ in. Pp. 282 + xii, with 111 illustrations. 1950. Munich and Berlin: Urban & Schwarzenberg. Rm. 16.

Non-gonococcal Urethritis. By A. H. HARKNESS, M.R.C.S., L.R.C.P. Joint Director of the Endell Street Clinic, St. Peter's and St. Paul's Hospitals (Institute of Urology); etc. $6\frac{7}{8} \times 9\frac{5}{8}$ in. Pp. 424 + xii, with 167 illustrations, 73 in colour. 1950. Edinburgh: E. & S. Livingstone Ltd. 52s. 6d.

The Breast. Edited by F. D. SANER, M.B., B.Ch. (Camb.), F.R.C.S. (Eng.), Surgeon, Royal Northern Hospital. 6×9 in. Pp. 316 + xii, with 193 illustrations, some in colour. 1950. Bristol: John Wright & Sons Ltd. 45s.

Essential Urology. By FLETCHER H. COLBY, M.D., Chief of the Urological Service. Massachusetts General Hospital; etc. 6×9 in. Pp. 580 + x, with 342 illustrations. 1950. Baltimore: The Williams & Wilkins Co. (London: Baillière, Tindall & Cox.) 61s. 6d.

Spezielle Chirurgische Diagnostik (De Quervain). Edited by Dr. KARL LENGGENHAGER, Bern. Tenth edition. $6\frac{1}{2} \times 10$ in. Pp. 767 + xii, with 956 illustrations, some coloured. 1950. Berlin: Springer. Price not stated.

La Chirurgie à Deux Equipes dans le Traitement des Cancers pelviens. By A. AMELINE, J. HUGUIER, P. MOYSE, and Y. CHATAIN. $6 \times 9\frac{1}{2}$ in. Pp. 160, with 62 illustrations. 1950. Paris: Librairie Arnette. Fr. 50.

Essentials of Urology. By J. C. AINSWORTH-DAVIS, M.A., M.D., B.Ch. (Cantab.), F.R.C.S. (Eng., and Edin.), Urological Surgeon, The Bolingbroke Hospital, London; etc. $5\frac{5}{8} \times 8\frac{3}{4}$ in. Pp. 734 + xii, with 512 illustrations. 1950. Oxford: Blackwell Scientific Publications. 50s.

An Introduction to Pathology. By G. PAYLING WRIGHT, D.M., F.R.C.P., Professor of Pathology, Guy's Hospital Medical School, University of London. $5\frac{7}{8} \times 8\frac{3}{4}$ in. Pp. 569 + x, with a large number of illustrations. 1950. London: Longmans Green & Co. Ltd. 30s.